

**Sudden Infant Death Syndrome Training
for Public Health Professionals
California SIDS Program
April 18, 2013**

**Sudden Infant Death Syndrome:
Overview of Current
Theories and Research**

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Angeles**

No Conflicts of Interest to Disclose

The painting depicts King Solomon seated on a throne, surrounded by a crowd of people. A woman in a red dress is kneeling in prayer, holding a dead child. Another woman in a green dress is standing and gesturing towards the king. The scene is set in a grand, classical-style interior with a checkered floor and a dog sniffing the dead child. The text is overlaid on the scene.

“And this woman's son
died in the night ...”

1 Kings 3: 19
(950 B.C.)

Antoon Claeissens, *The Judgment of Solomon*, ~1600.

LAPSE OF TIME FROM MOMENT WHEN LAST SEEN ALIVE TO THE
DISCOVERY OF DEATH (96 Cases)

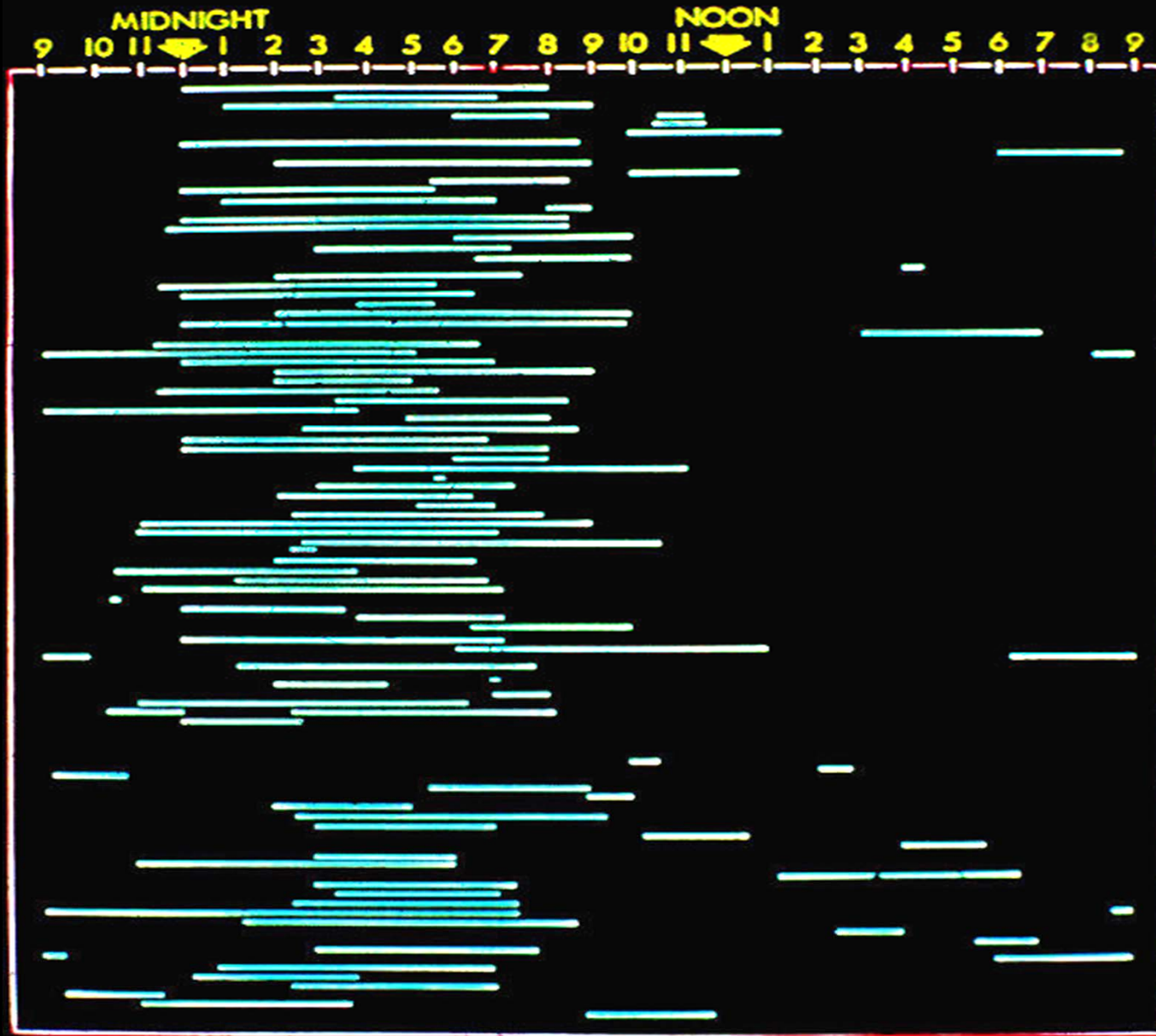


Figure Courtesy of Doctor Maria Valdes-Dapena

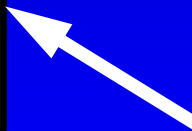
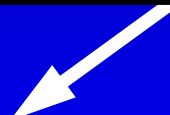
**Sudden Death
of an Infant**

**Emergency
Responders**

**Coroner's
Investigation**

**Determination of
Cause of Death**

Autopsy

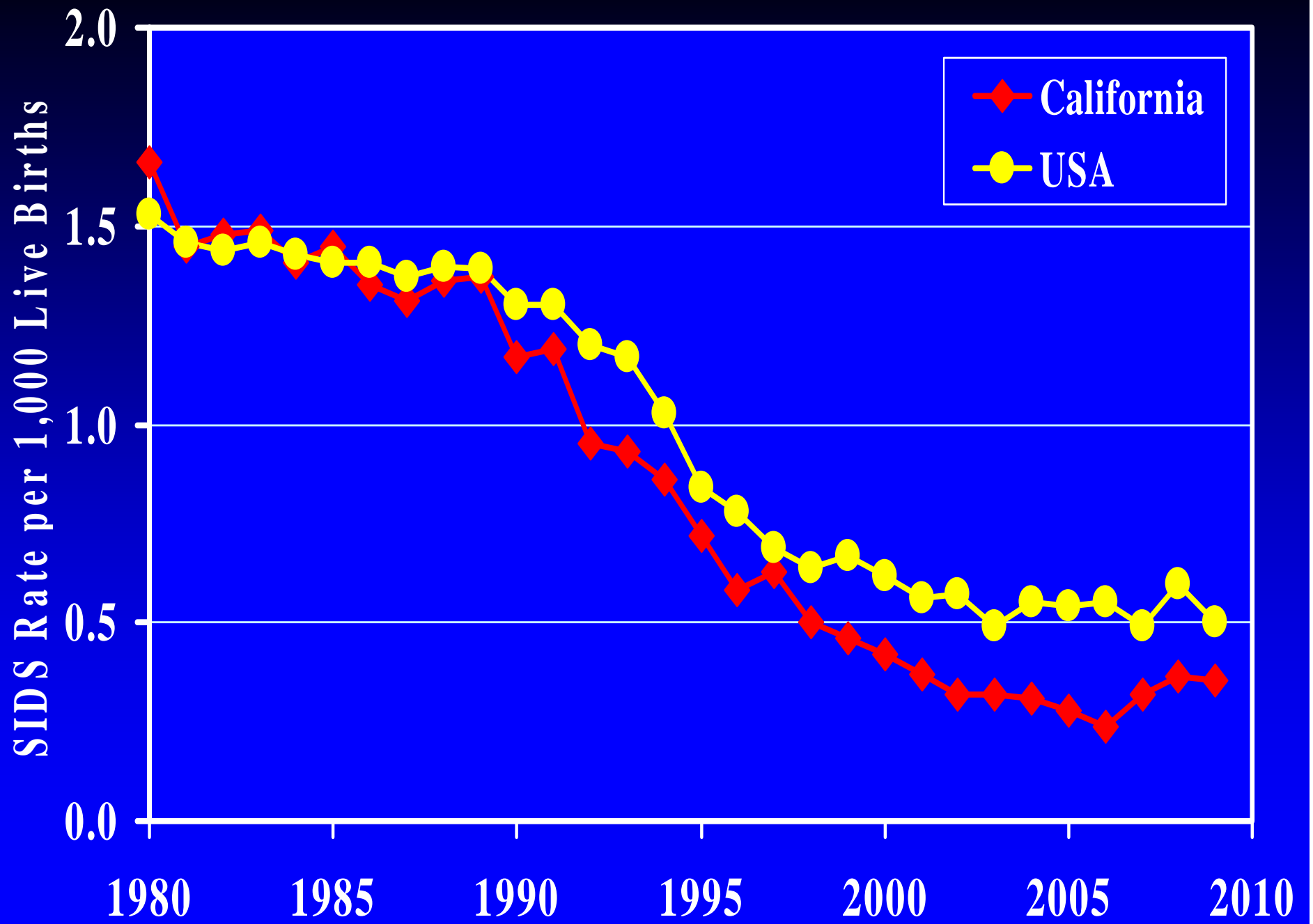


Sudden Infant Death Syndrome

The sudden unexpected death of an infant, under one-year of age, with onset of the fatal episode apparently occurring during sleep, that remains unexplained after a thorough investigation, including performance of a complete autopsy, and review of the circumstances of death and the clinical history.

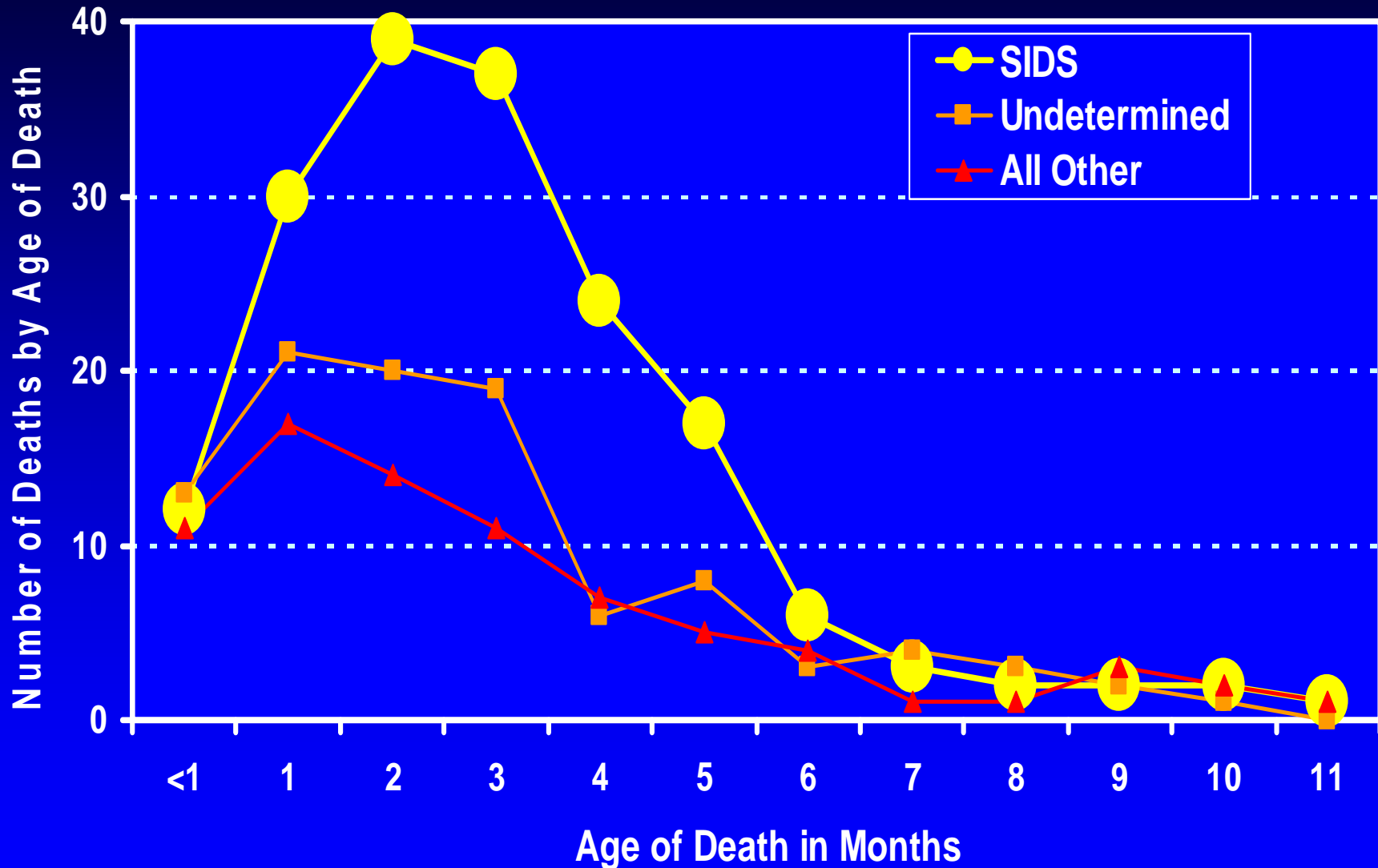
Krous, H.F., J.B. Beckwith, R.W. Byard, T.O. Rognum, T. Bajanowski, T. Corey, E. Cutz, R. Hanzlick, T.G. Keens, and E.A. Mitchell.

Pediatrics, 114: 234-238, 2004.





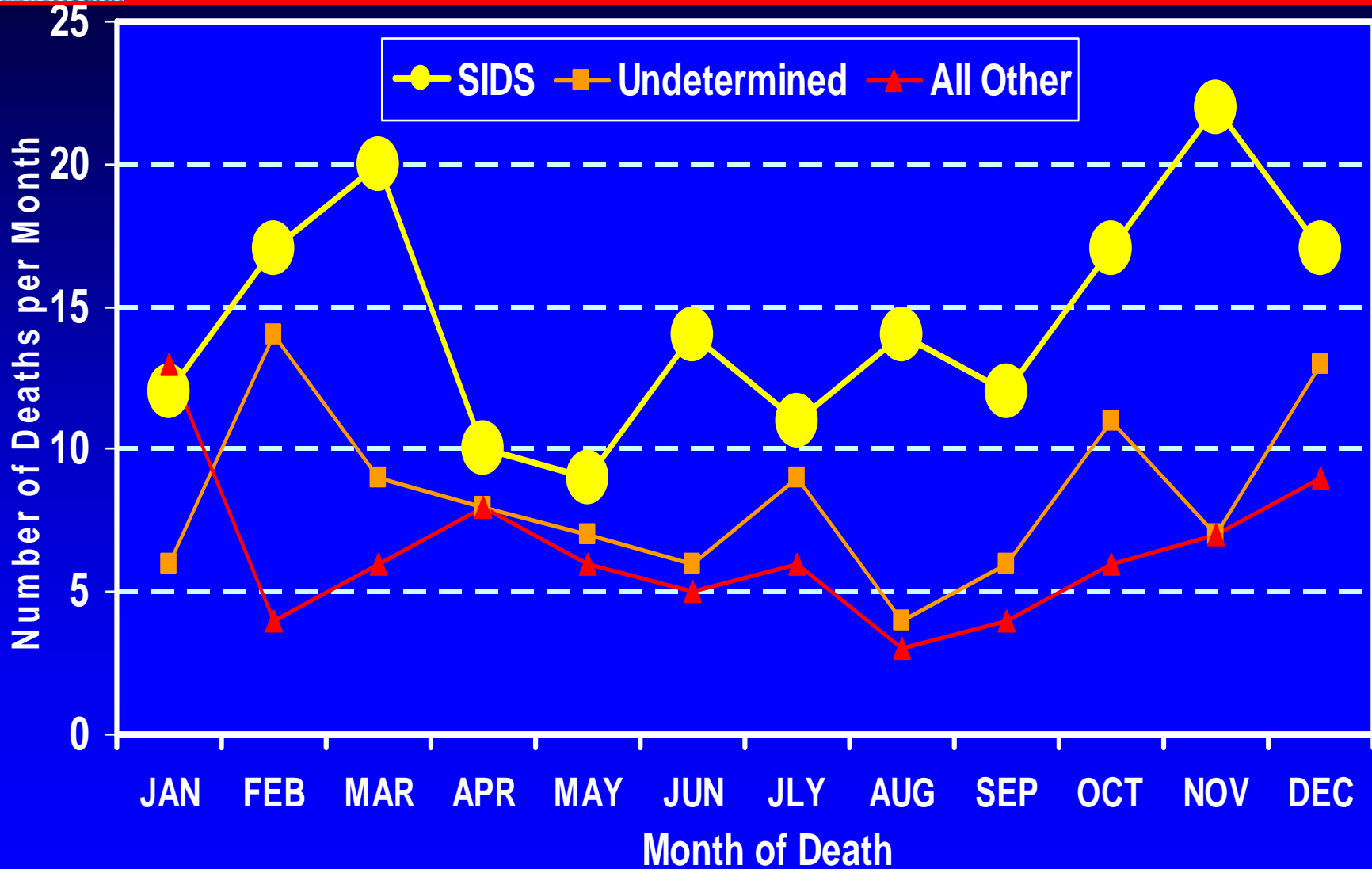
Infant Deaths by Age of Death California 2003



California 2002-2003 Birth & 2003 Death Statistical Master Files & SUID Database, 2003.
California Department of Health Services, MCAH/OFP, September 2005.



Infant Deaths by Month of Death California 2003

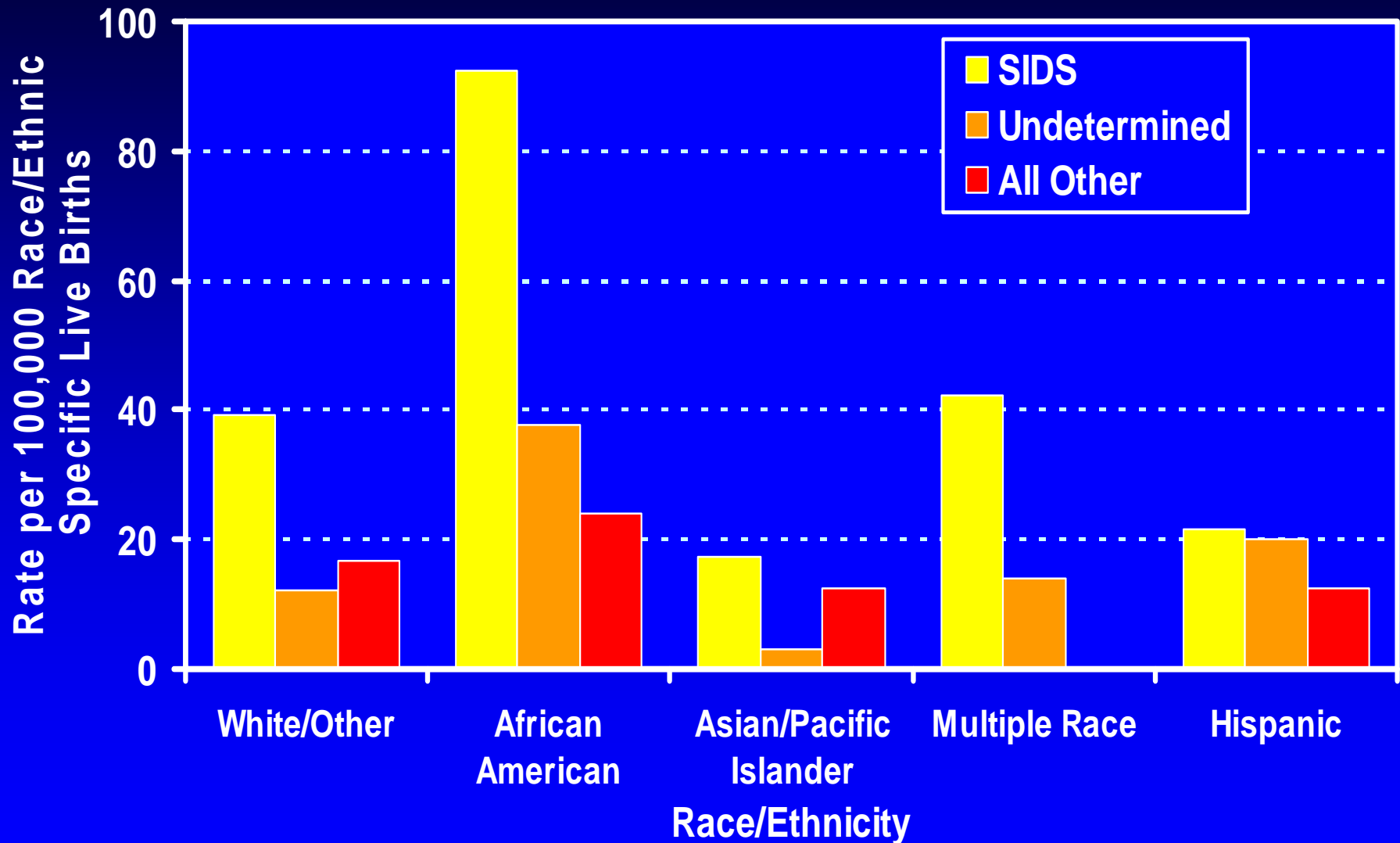


California 2002-2003 Birth & 2003 Death Statistical Master Files & SUID Database, 2003.
California Department of Health Services, MCAH/OFP, September 2005.



Infant Deaths by Race/Ethnicity

California 2003 SUID Data



California 2002-2003 Birth & 2003 Death Statistical Master Files & SUID Database, 2003.
California Department of Health Services, MCAH/OFP, September 2005.

SIDS Autopsy Findings

- **No identifiable cause of death.**
- **No signs of severe illness.**
- **No signs of significant stress.**

How Are We to Understand SIDS?

Imagine a car driving up a steep mountain road.

The car has stopped.

Why can't the car continue up the hill?

Modified after Professor Jacopo P. Mortola. McGill University.

How Are We to Understand SIDS?

Imagine a car driving up a steep mountain road.

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Why can't the car continue up the hill?

- **Medical Model.**
 - All four tires are flat.
 - Identify the problem.
 - Find a solution to the problem.
 - Fix the problem.

Modified after Professor Jacopo P. Mortola. *McGill University.*

Medical Model of SIDS

- **Cardiac causes.**
- **Respiratory causes.**
- **Arousal disorders.**
- **Metabolic disorders.**
- **Infections.**
- **Vitamin deficiency.**
- **Environmental toxins.**

How Are We to Understand SIDS?

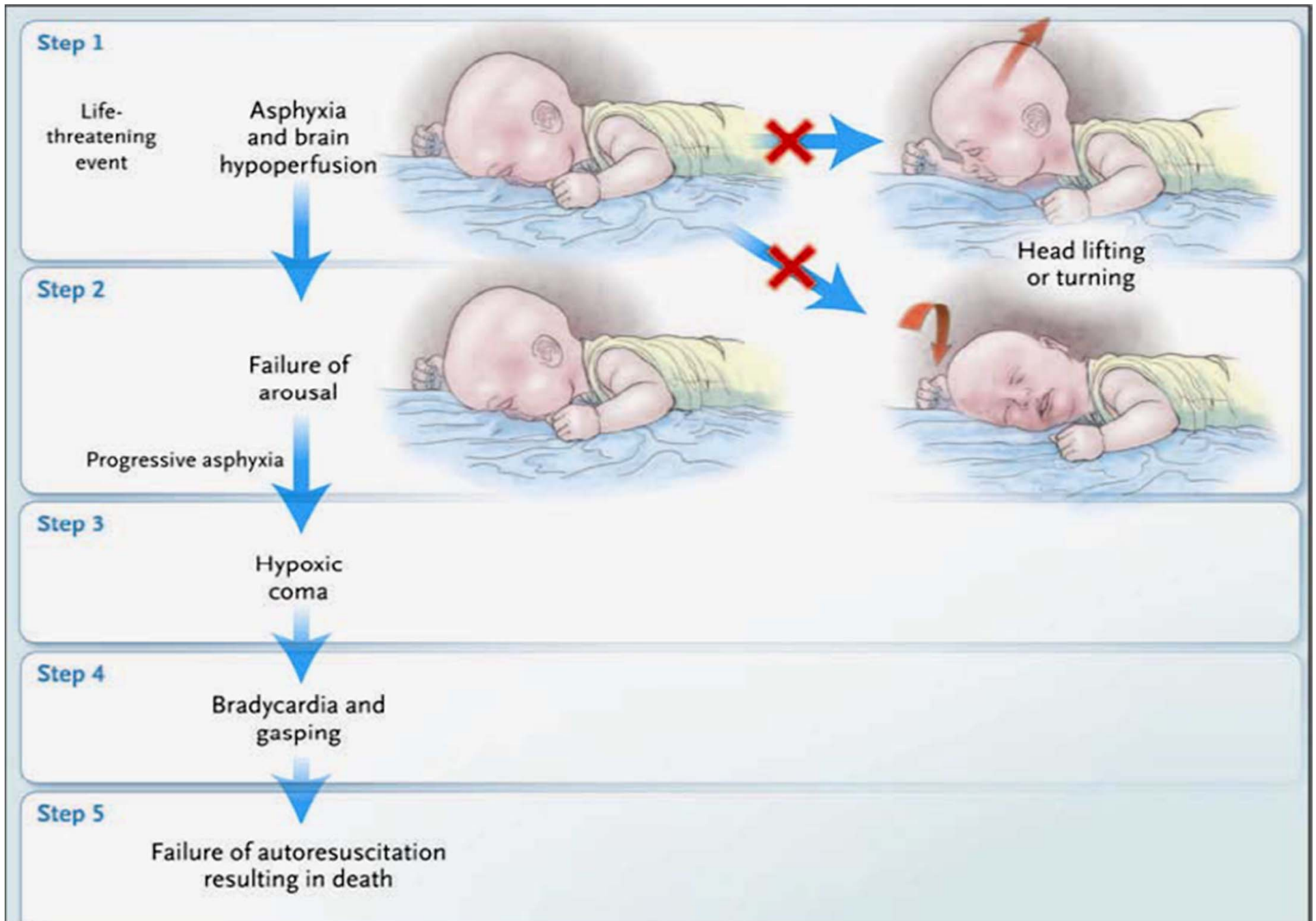
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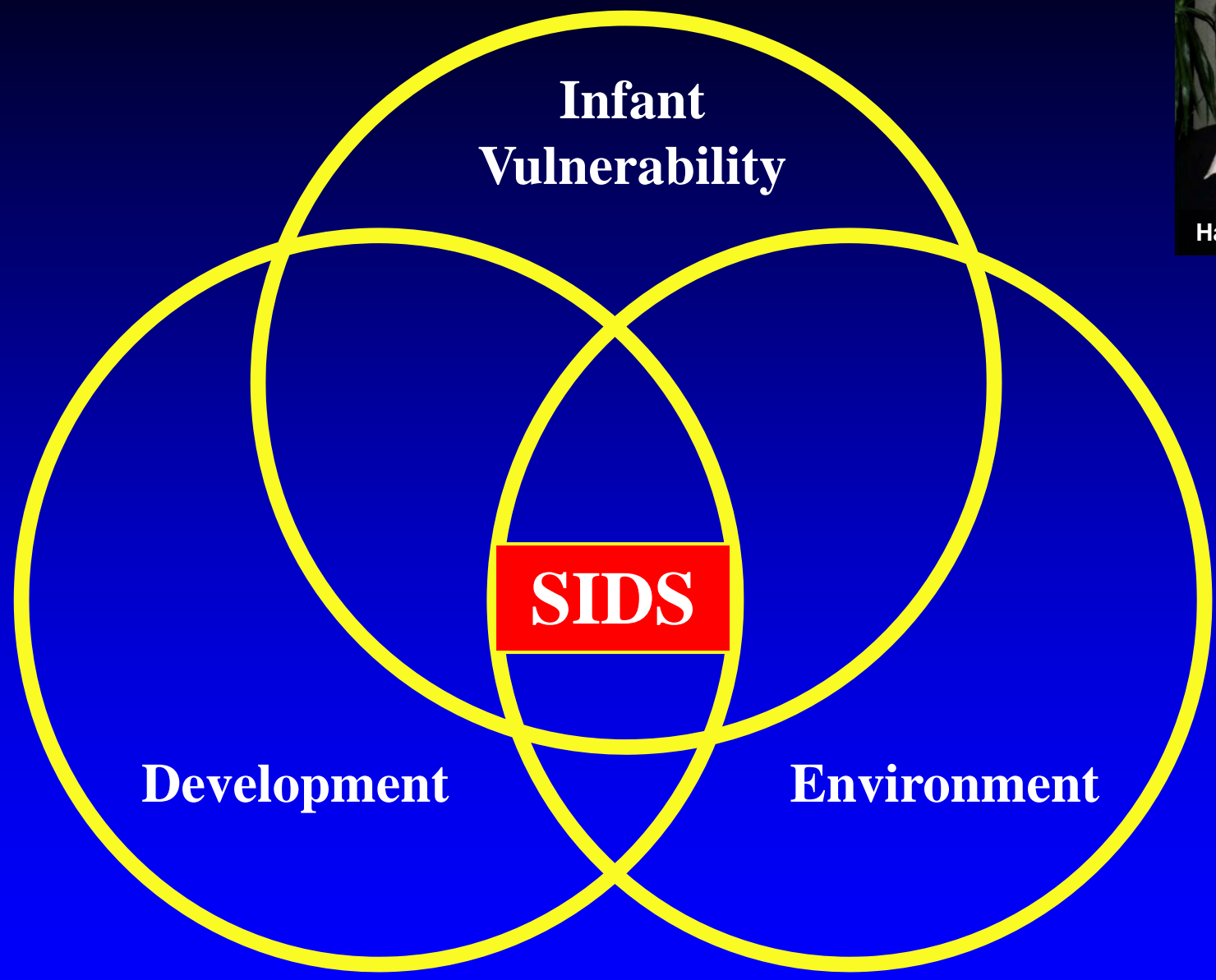
Why can't the car continue up the hill?

- **A New Way of Thinking.**
 - There are too many passengers.
 - The engine is not powerful enough.
 - The road is too rocky.
 - The road is too steep.

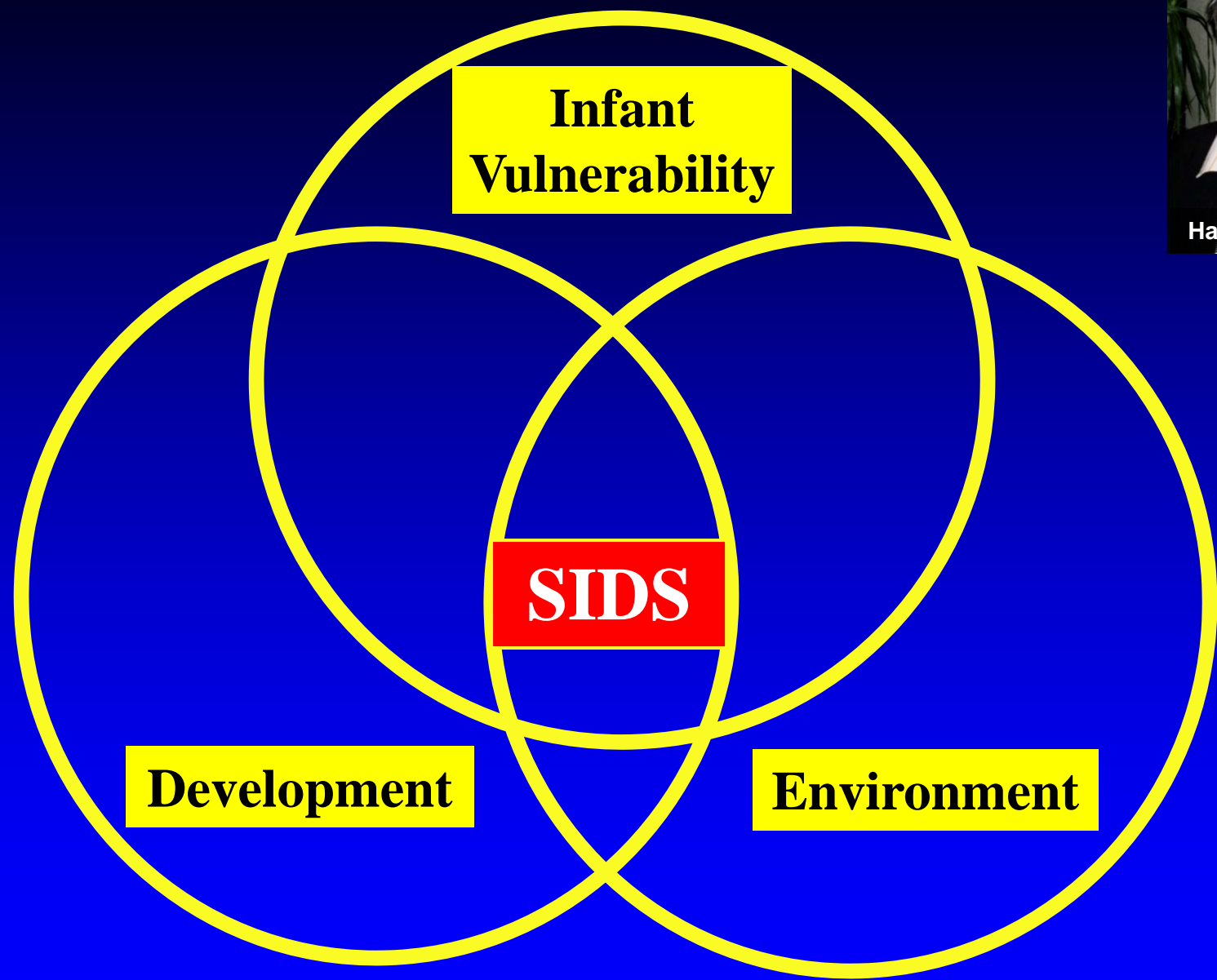
Modified after Professor Jacopo P. Mortola. McGill University.



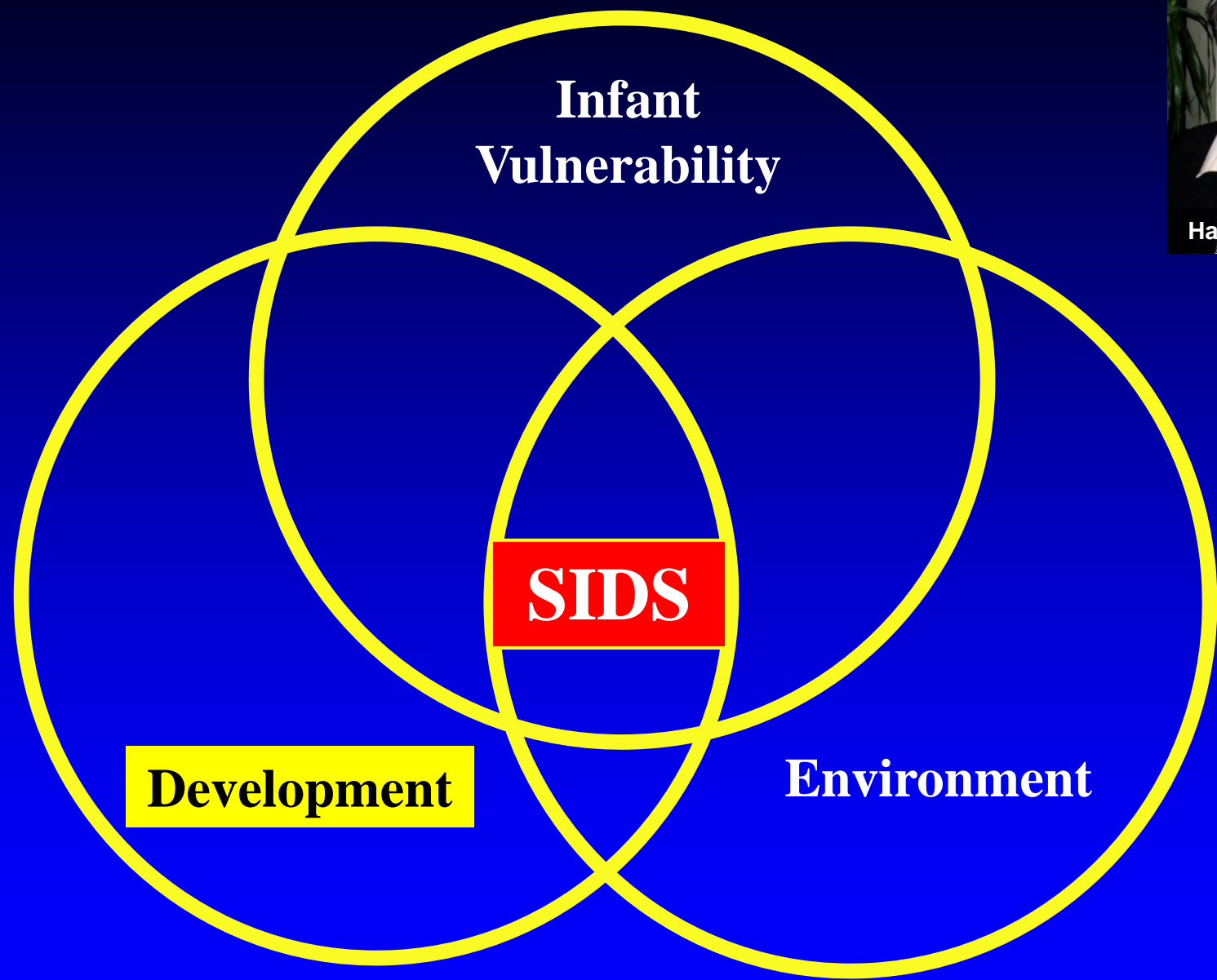
Kinney, H.C., and B.T. Thach. *N. Eng. J. Med.*, 361: 795-805, 2009.



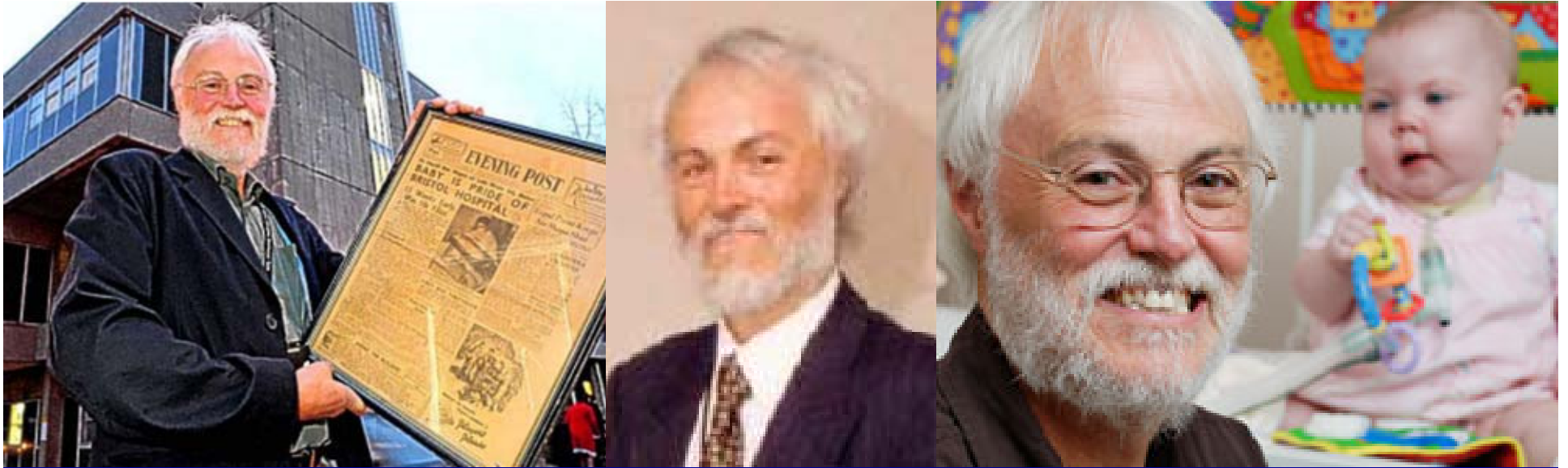
Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



- **Any system in transition is intrinsically unstable.**
- **Infant cardiorespiratory physiology undergoes rapid changes in the first 3-6 months of life.**
- **Thus, infant physiological responses are immature and do not function optimally.**

Fleming, P.J., M.R. Levine, A.M. Long, and J.P. Cleave. Postnatal development of respiratory oscillations. *Ann. N.Y. Acad. Sci.*, 533: 305-313, 1988.

The CHIME Study

- **Clinical Sites.**
 - **Los Angeles, California.**
 - **Chicago, Illinois.**
 - **Honolulu, Hawaii.**
 - **Cleveland, Ohio.**
 - **Toledo, Ohio.**
- **Clinical Trial Operation Center.**
- **Data Coordinating and Analysis Center.**
- **NICHD.**

Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.

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Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.

CHIME -- Study Plan

| | |
|-----------------------------|---|
| Healthy Term Infants | Home monitoring up to 66 wks PCA (age 6 months). |
| Preterm Infants | Home monitoring up to 56 wks PCA (age 4 months). |
| ALTE Infants | Until infant has no real alarms for 3-months. |
| SIDS Siblings | Until 66 wks PCA, or 4 wks past age of death of SIDS. |

Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.

The CHIME Home Monitor

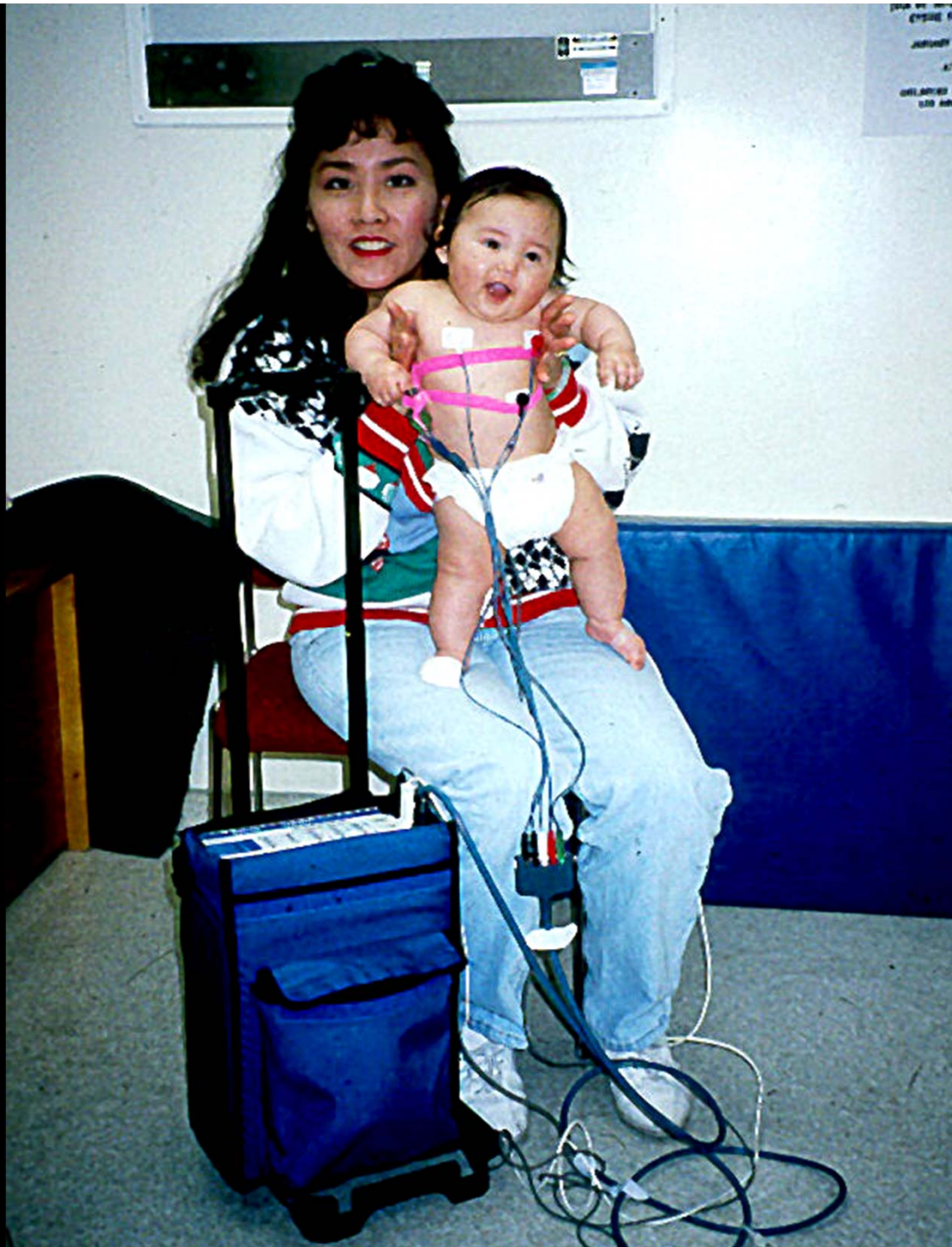
- Respiratory Inductance Plethysmography.
- Central and Obstructive Apneas.
- Electrocardiogram.
- Pulse Oximeter.
- Body Position.
- Computer to record events and normative data.

Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.

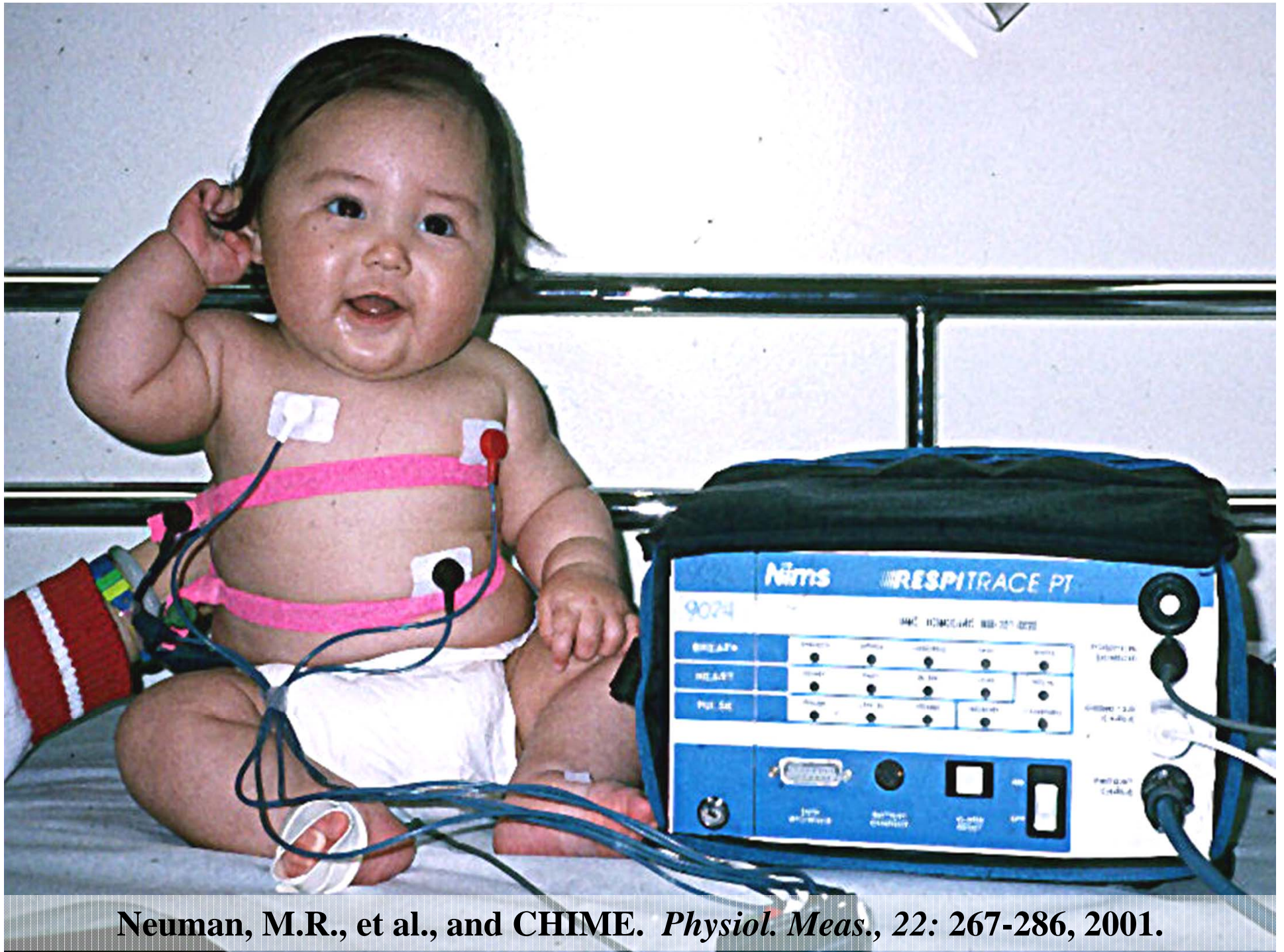
Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.



**The CHIME Home Monitor (*Non Invasive Monitoring Systems*, Miami, Florida, U.S.A.)
Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.**



*The
CHIME
Home
Monitor*



Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.

215 %Vt

Vt

215 %Vt

RC

215 %Vt

AB

5.00 mV

ECG

200 BM

HR

0.8M

100 %

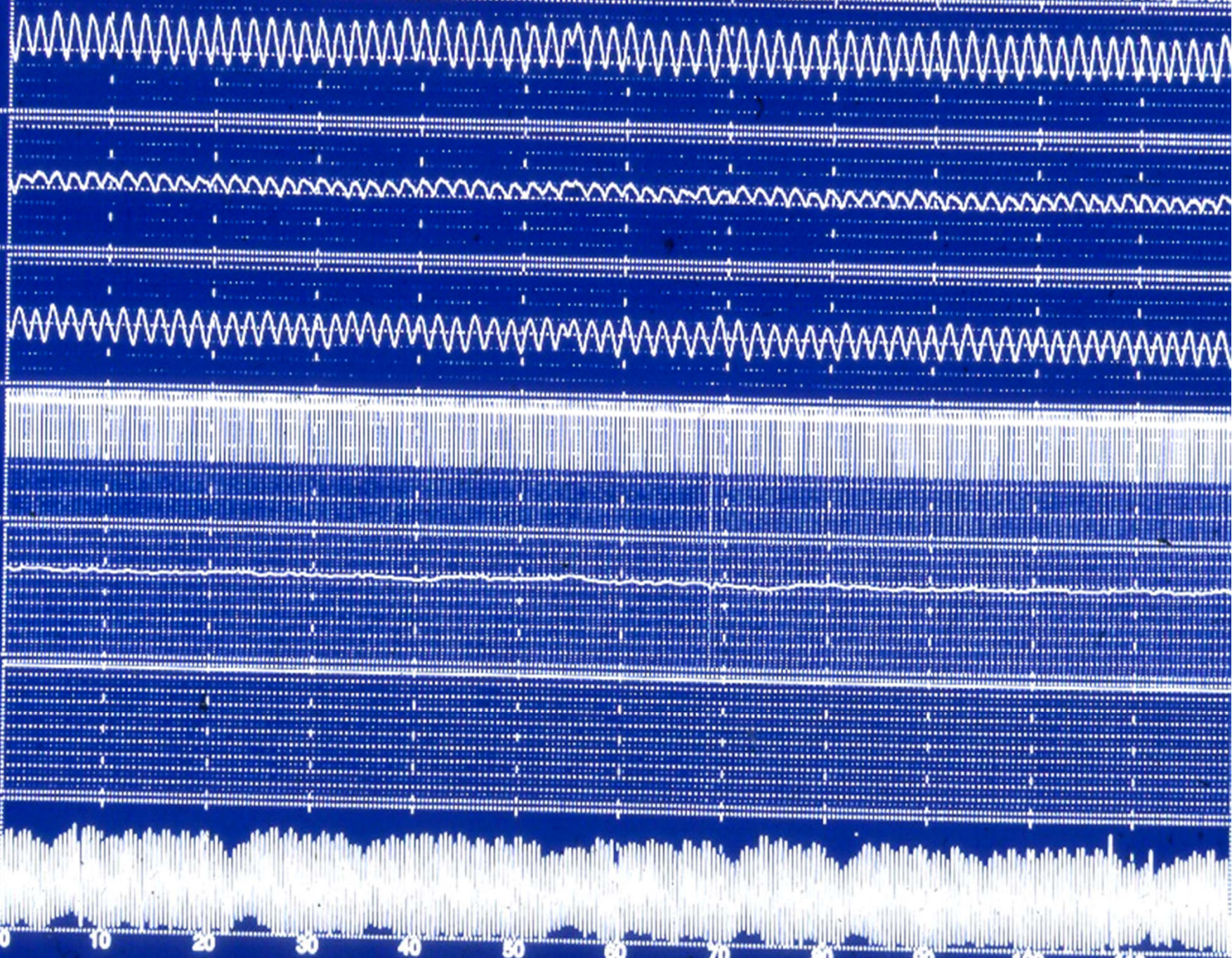
SaO2

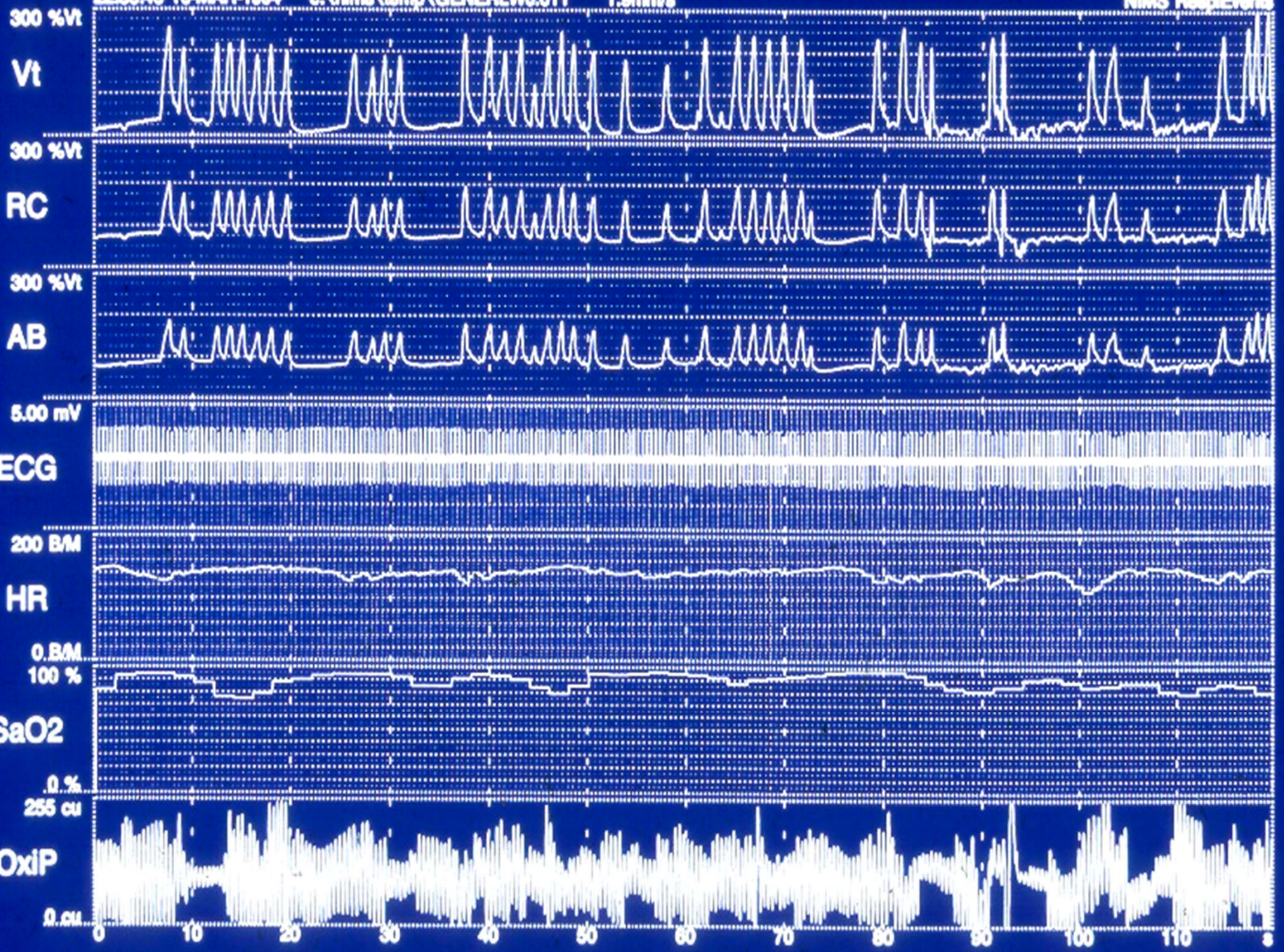
0.0 %

255 cu

OxiP

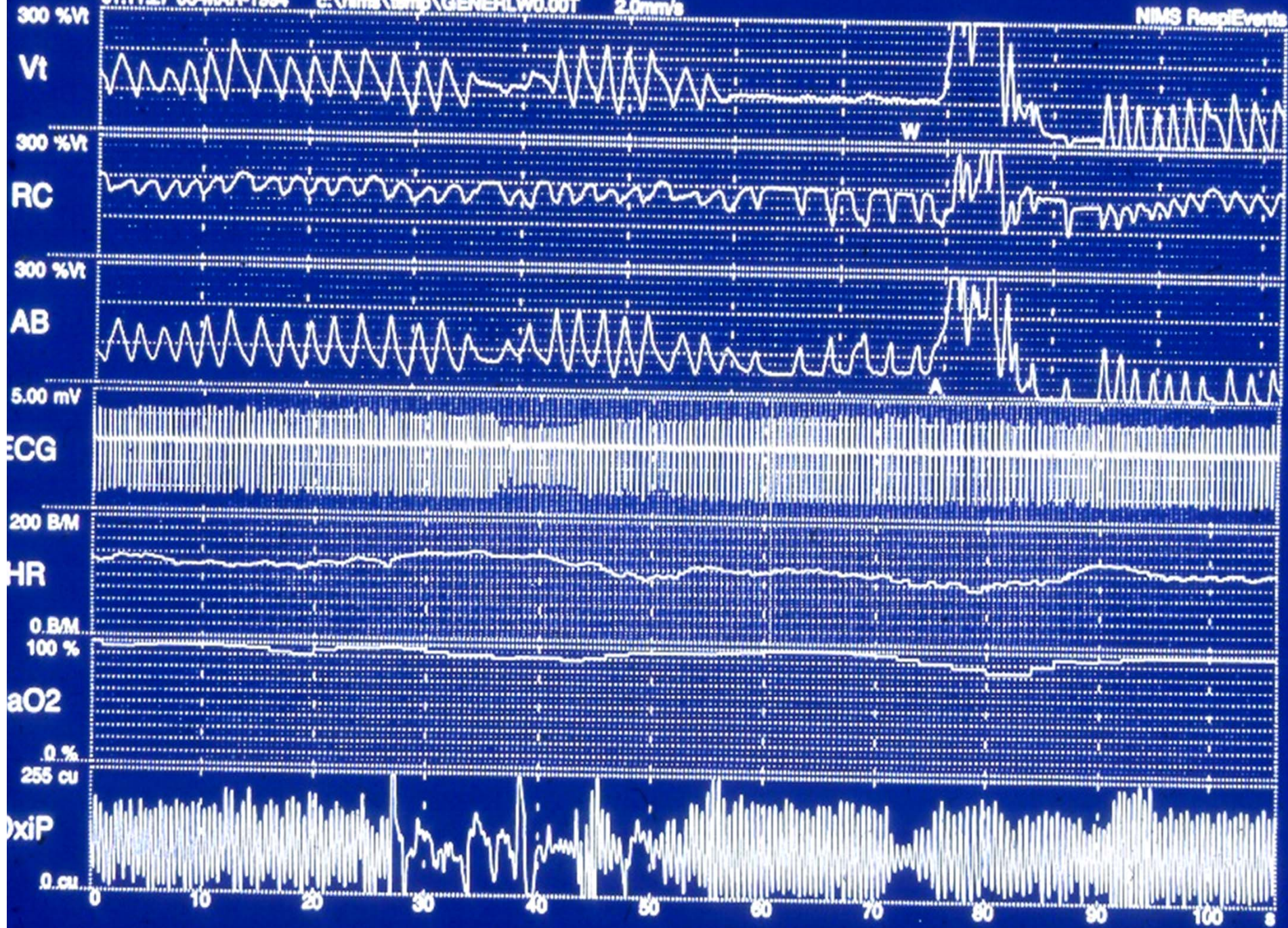
0.0 cu





01:11:27 08-MAR-1994 c:\nims\temp\GENERLW0.00T 2.0mm/s

NIMS RespEvents

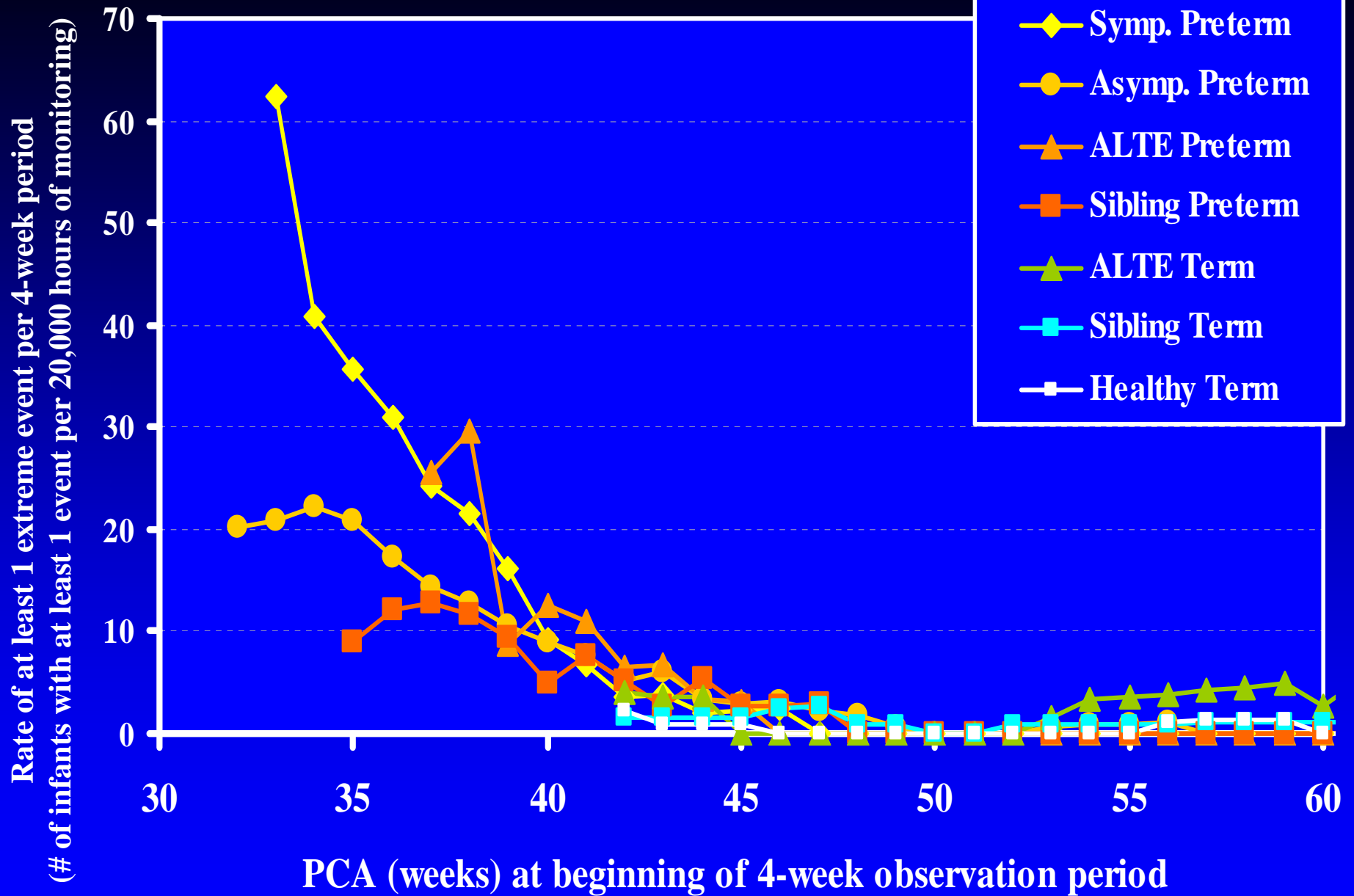


Oxygen Saturation in Healthy Infants During Sleep at Home

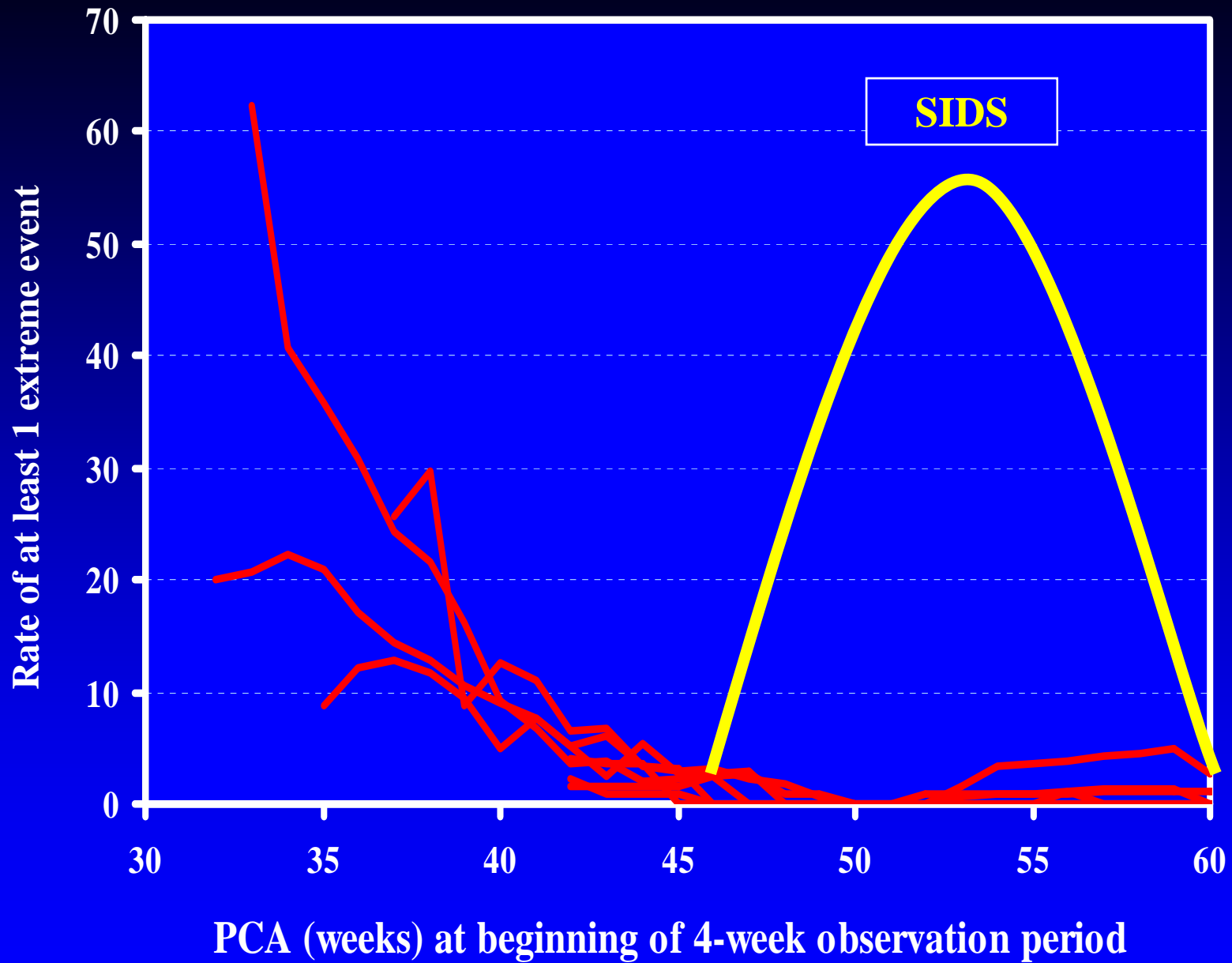


- Average baseline S_pO_2 was 97.9%, and did not change with age.
- Hypoxia ($S_pO_2 < 90\%$) occurred in 59% of infants.
- Hypoxia ($S_pO_2 < 90\%$) occurred 0.6% of epochs.
- Acute desaturations were most common in periodic breathing and short apneas.

Hunt, C.E., and CHIME. *J. Pediatr.*, 135: 580-586, 1999.

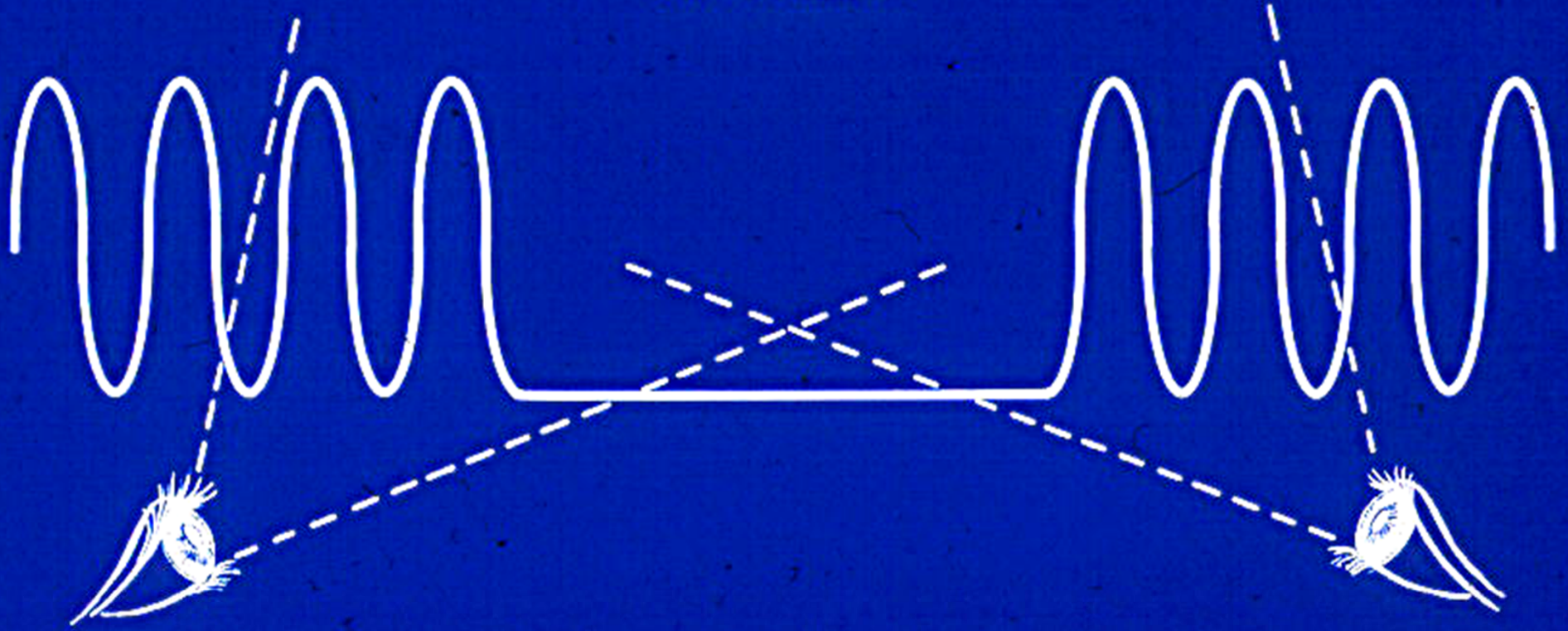


Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.

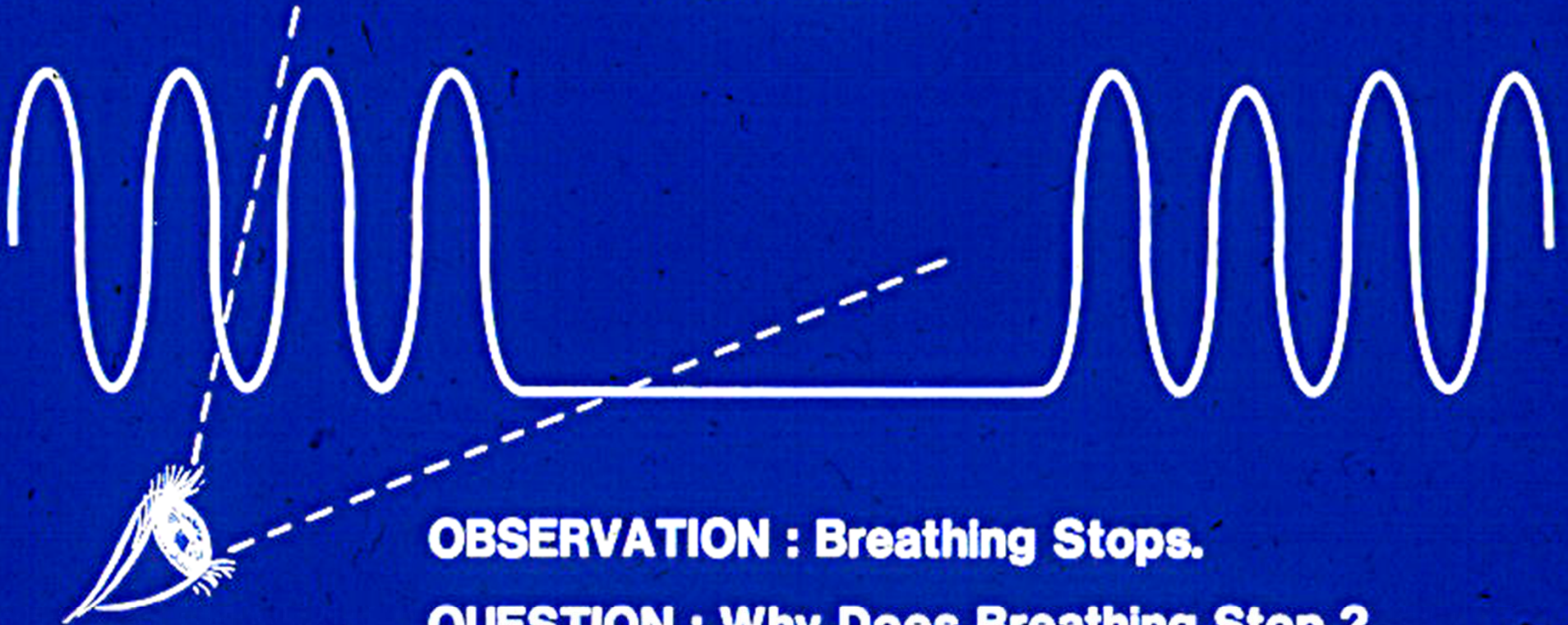


Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.

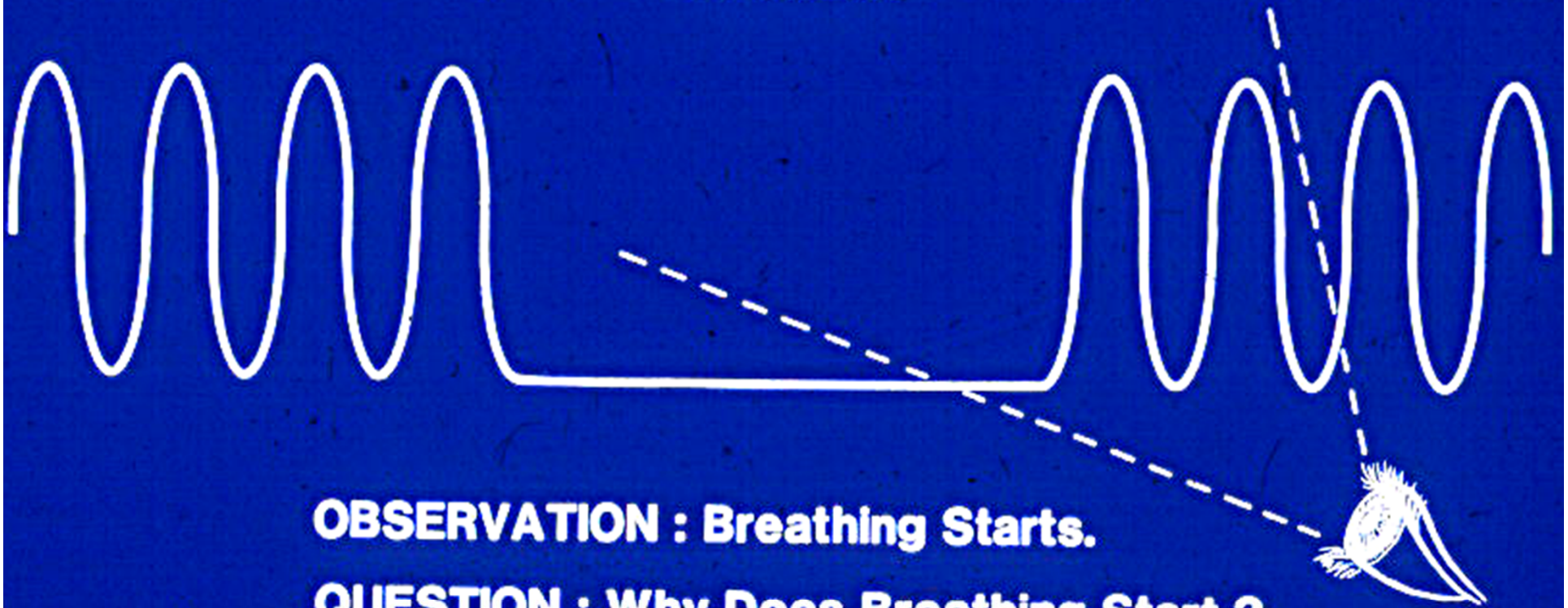
APNEA



APNEA



APNEA



OBSERVATION : Breathing Starts.

QUESTION : Why Does Breathing Start ?

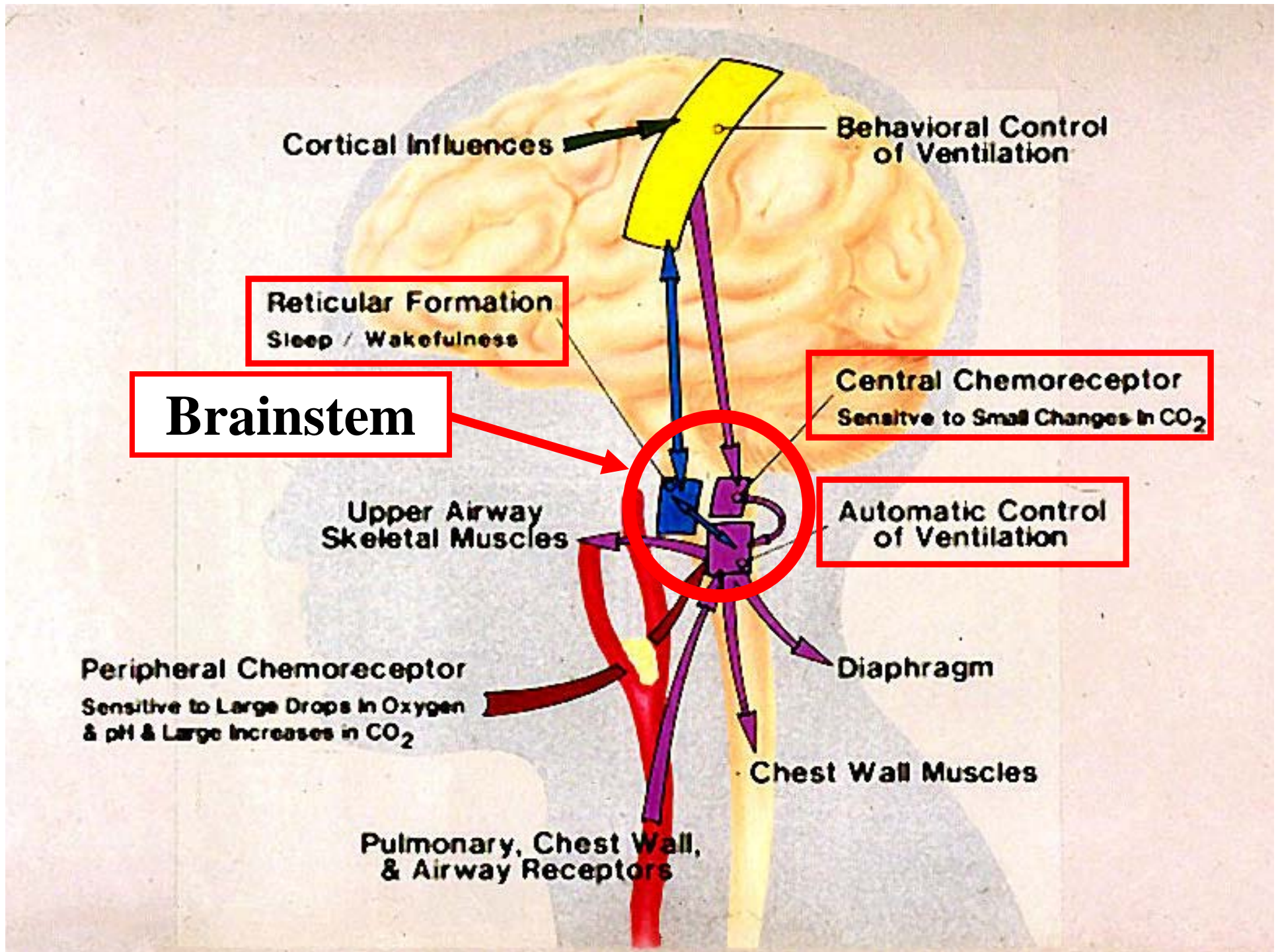
Arousal: A Protective Defense



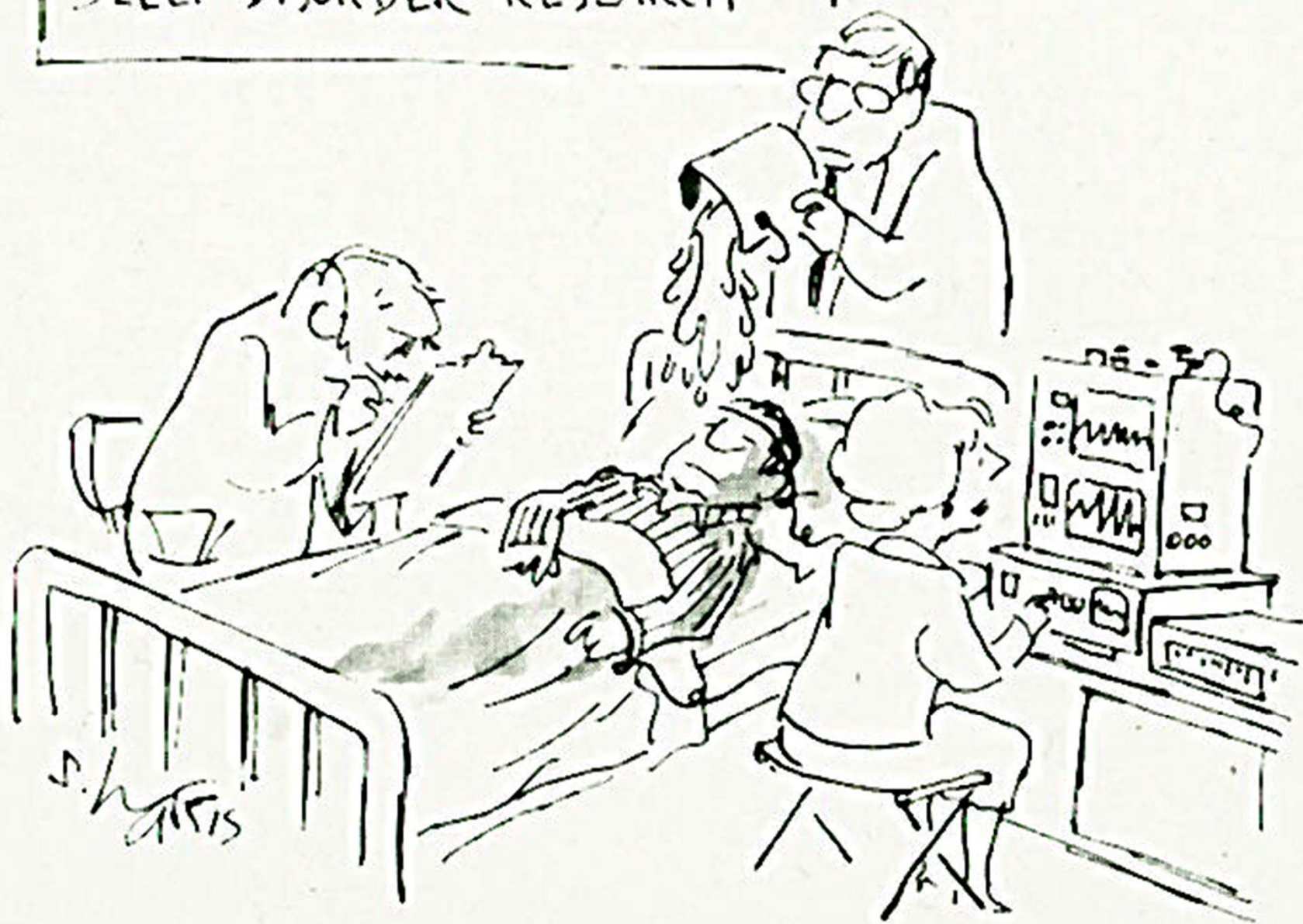
Professor Andre Kahn
1943-2004

- Arousal (waking up) is an important defense against danger-signaling stimuli during sleep.
- Immature breathing causes frequent apnea and hypoxia.
- Many SIDS researchers believe that failure to arouse in response to these may contribute to SIDS.

Arousal Mechanisms: The Andre Kahn Memorial Symposium.
9th SIDS International Conference. Yokohama, Japan. June 1-4, 2006.



SLEEP DISORDER RESEARCH

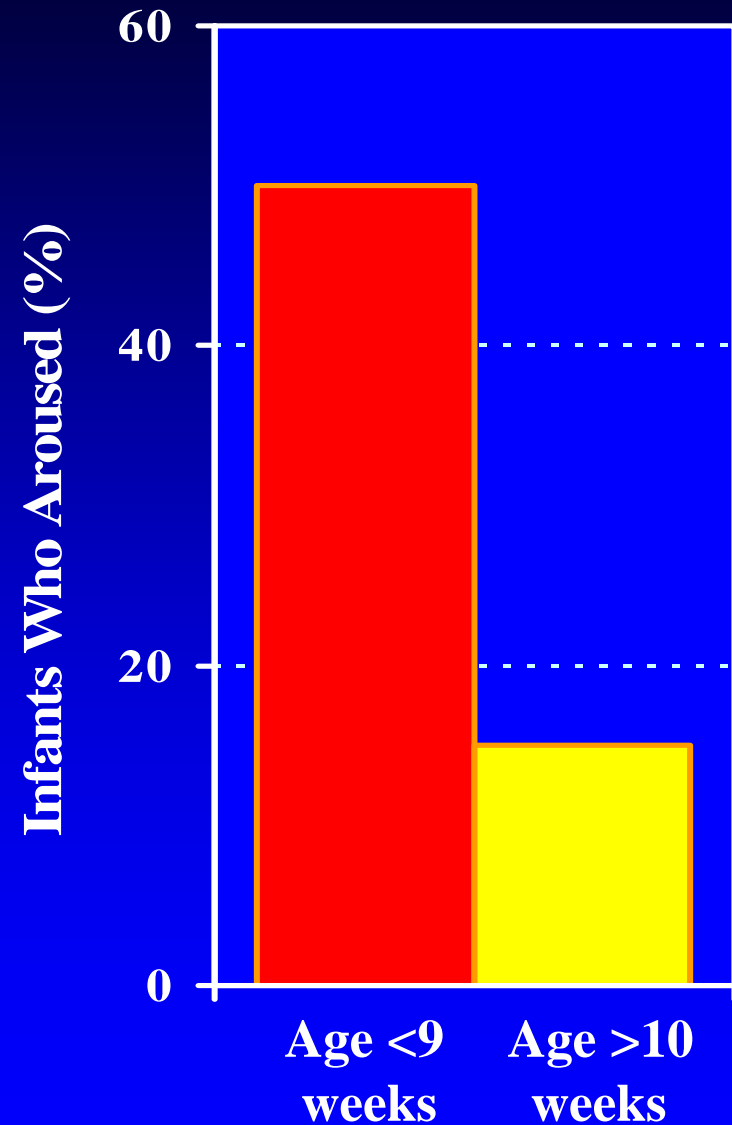
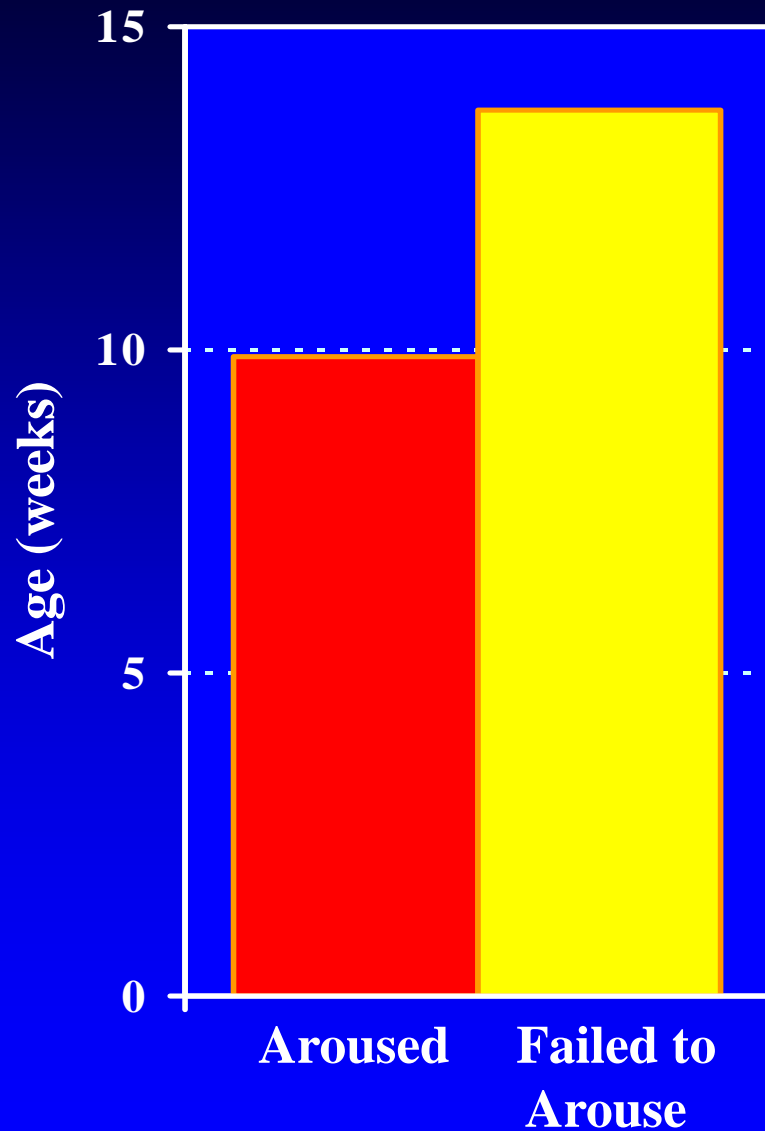




Davidson Ward, S.L., et al. *Pediatrics*, 89: 860-864, 1992.

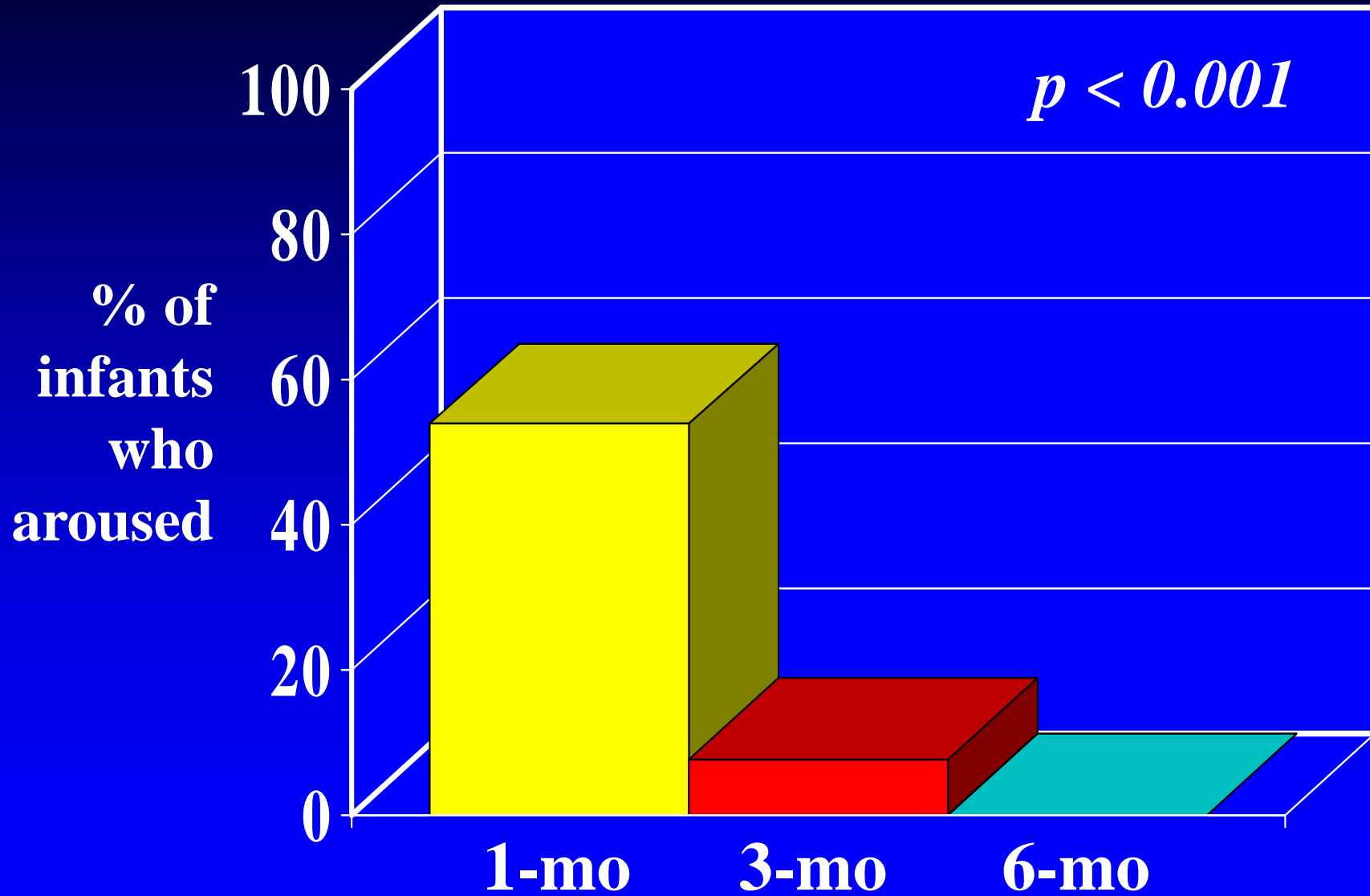
Hamutcu, R., et al. *Am. J. Respir. Crit. Care Med.*, 163(5): A953, 2001.

Hypoxic Arousal Response



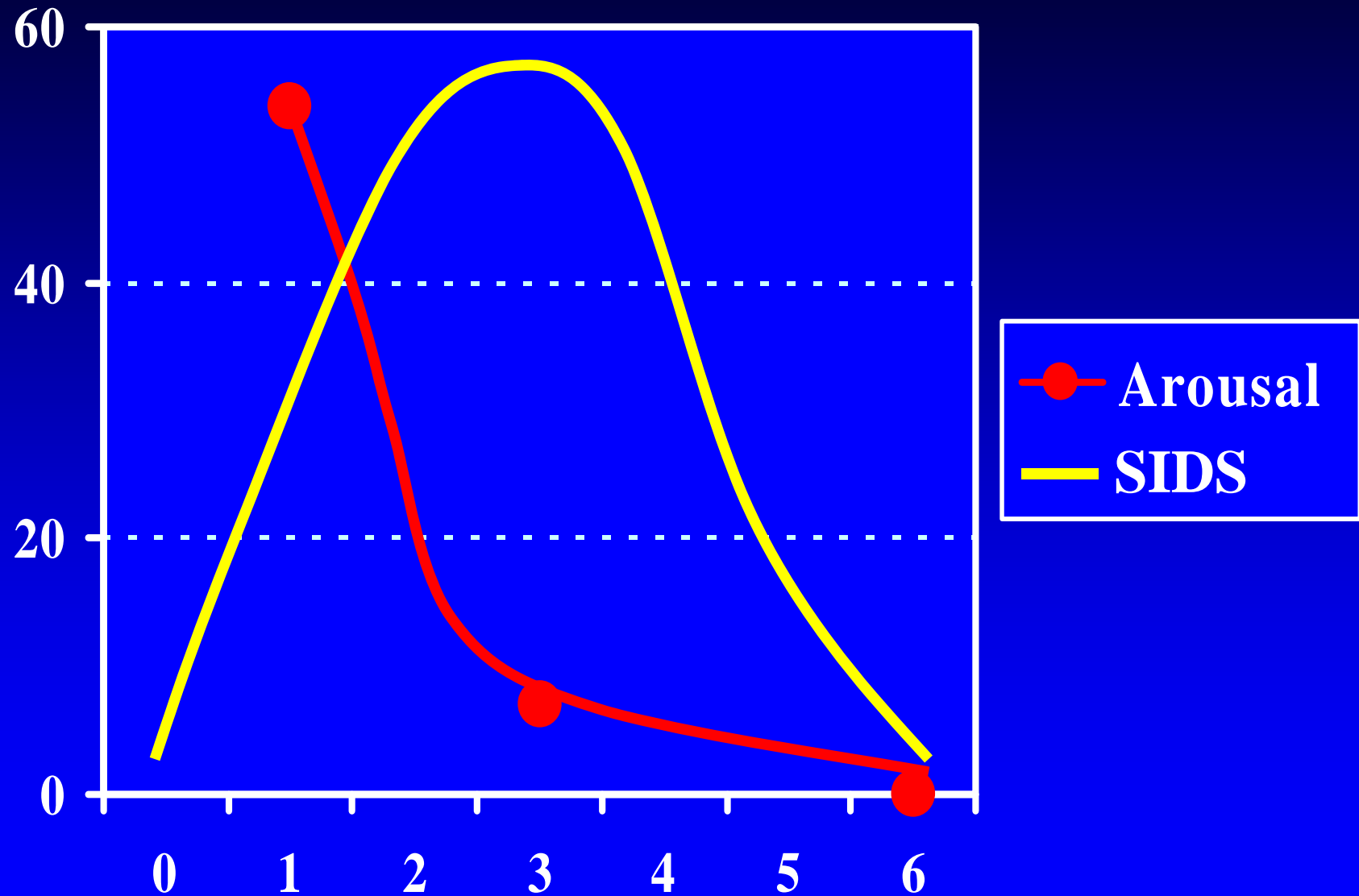
Davidson Ward, S.L., et al. *Pediatrics*, 89: 860-864, 1992.

Arousal to Hypoxia

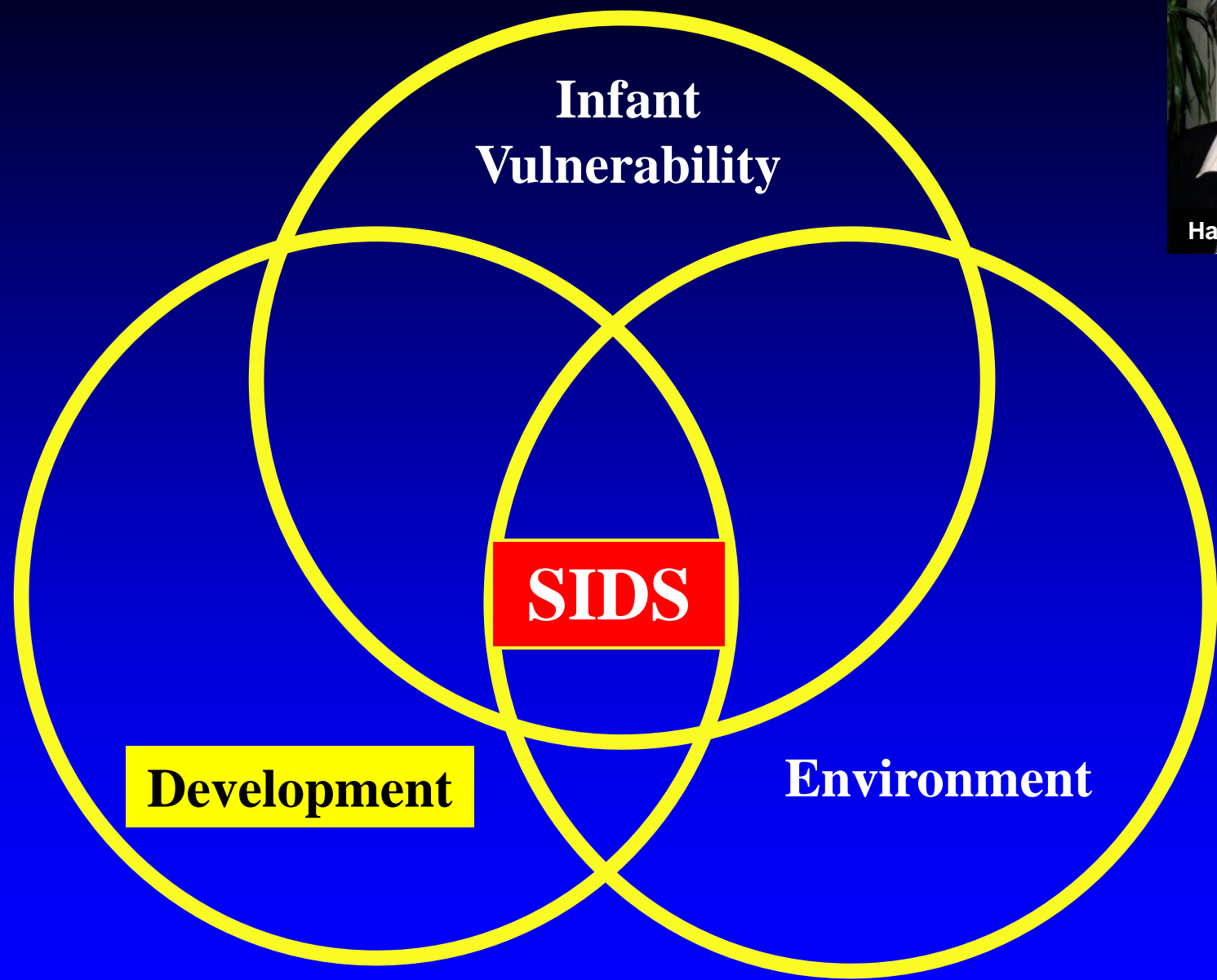


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Arousal to Hypoxia



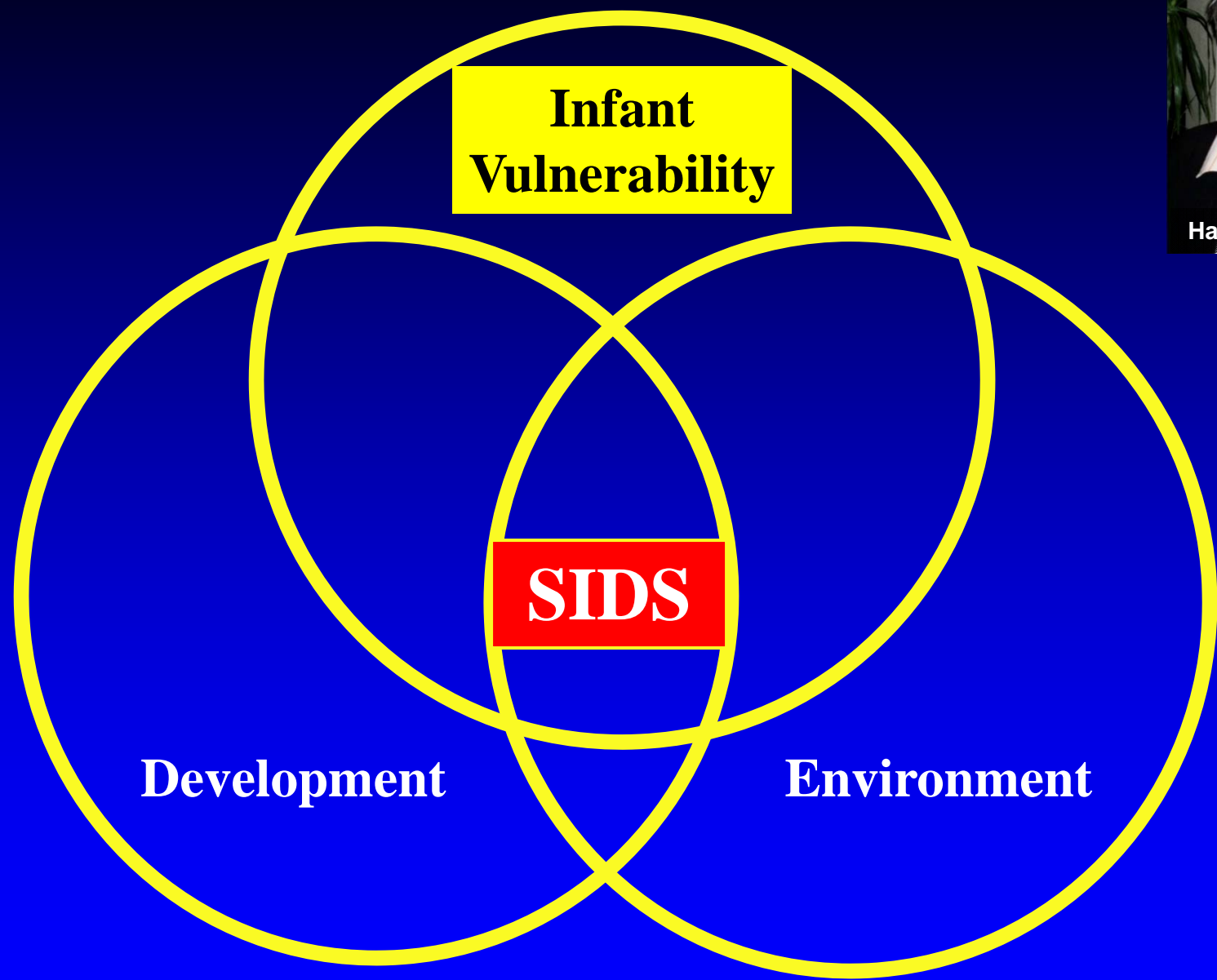
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Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



Hannah Kinney



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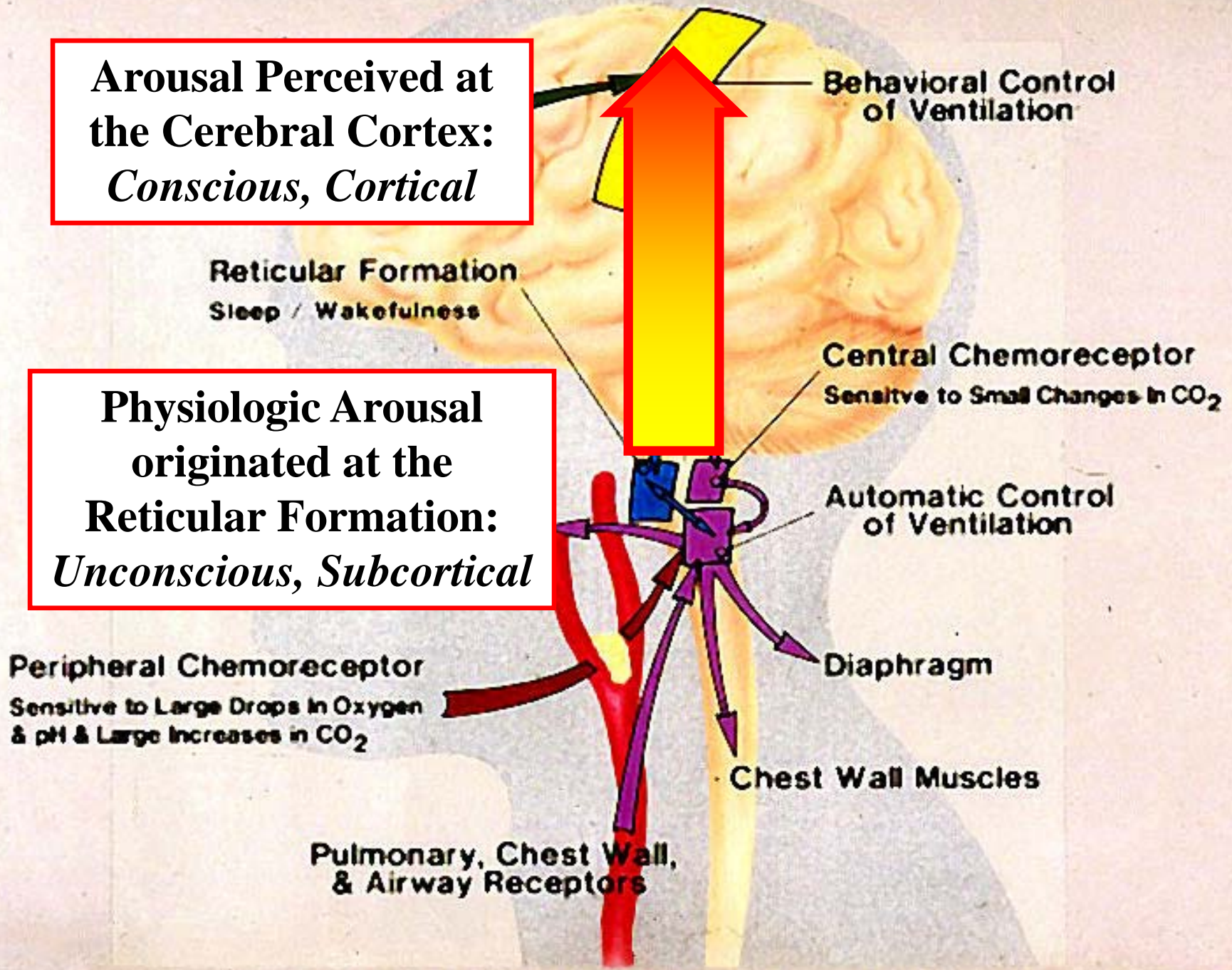
Spontaneous Arousals During Sleep

- On overnight PSG, 16 subsequent SIDS babies, compared to control infants, had:
 - ↓ total arousals during REM sleep ($p=0.29$).
 - ↓ cortical arousals ($p=0.39$).
 - ↑ subcortical arousals ($p=0.18$).
 - ↓ S_pO_2 preceding cortical arousals ($p<0.001$).
 - ↓ S_pO_2 preceding subcortical arousals ($p=0.13$).
- Results suggest incomplete arousal in SIDS.

Kato, I., P. Franco, S. Scaillet, J. Grosswasser, H. Togari, and A. Kahn.
Nagoya City University, Nagoya, Japan, and Free University of Brussels.
9th SIDS International Conference, Yokohama, Japan, June 1-4, 2006.

**Arousal Perceived at
the Cerebral Cortex:
*Conscious, Cortical***

**Physiologic Arousal
originated at the
Reticular Formation:
*Unconscious, Subcortical***



**Arousal Perceived at
the Cerebral Cortex:
*Conscious, Cortical***

Behavioral Control
of Ventilation

**Incomplete
Arousal in SIDS**

Reticular Formation
Sleep / Wakefulness

**Physiologic Arousal
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Reticular Formation:
*Unconscious, Subcortical***

Central Chemoreceptor
Sensitive to Small Changes in CO₂

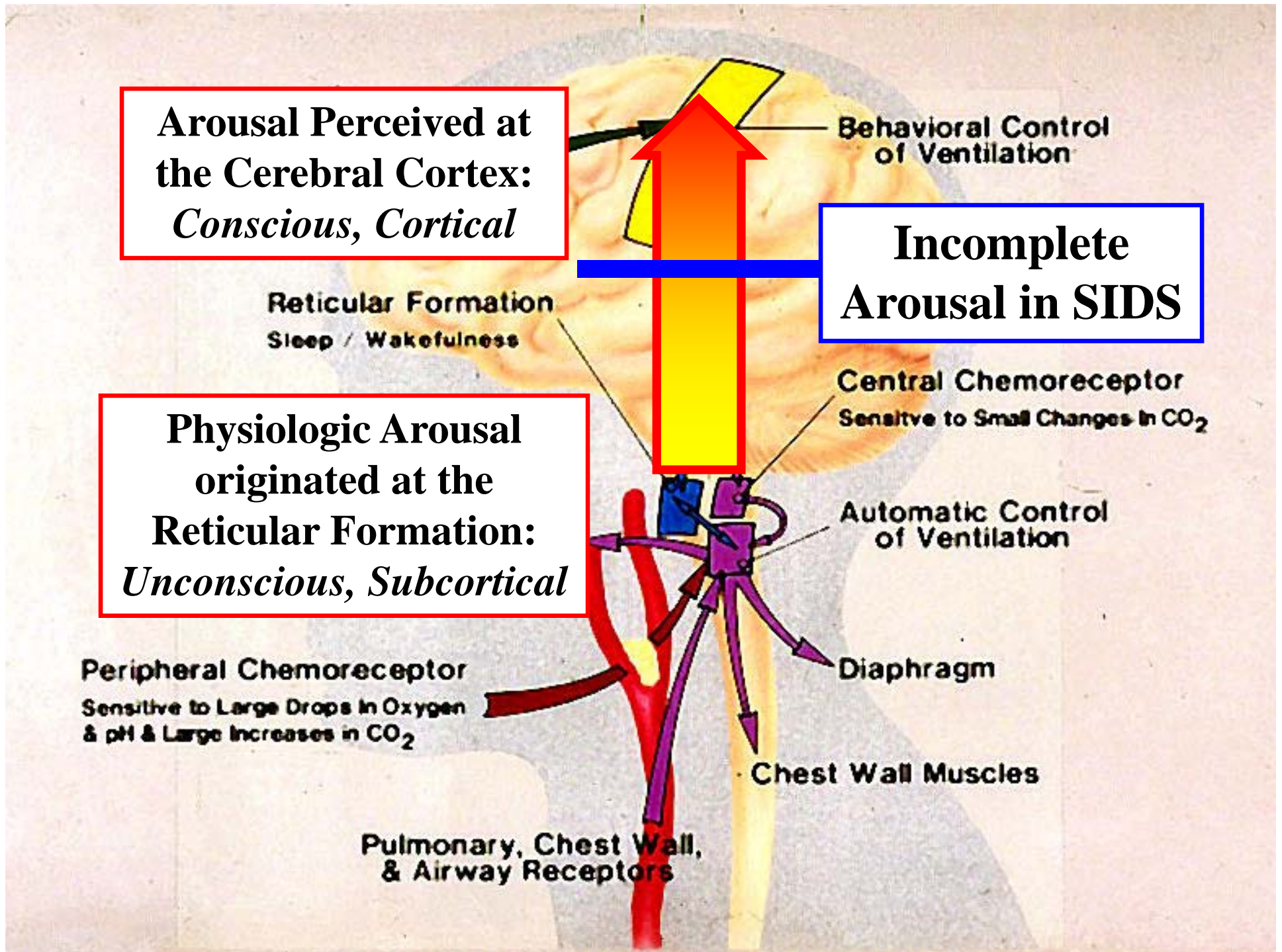
Automatic Control
of Ventilation

Peripheral Chemoreceptor
Sensitive to Large Drops in Oxygen
& pH & Large Increases in CO₂

Diaphragm

Chest Wall Muscles

Pulmonary, Chest Wall,
& Airway Receptors



Cardiorespiratory Interaction

- Neurologic control of respiratory and cardiac function are linked through autonomic nervous system function.
- Patients with cardiorespiratory disorders exhibit neuronal damage to brain areas involved in cardiorespiratory control.
- Could this cause autonomic nervous system damage, leading to SIDS?

Harper, R.M, et al. *J. Neurophysiol.* 93: 1647-1658, 2005.

Kumar, R., et al. *J. Compar. Neurol.*, 487: 361-371, 2005.

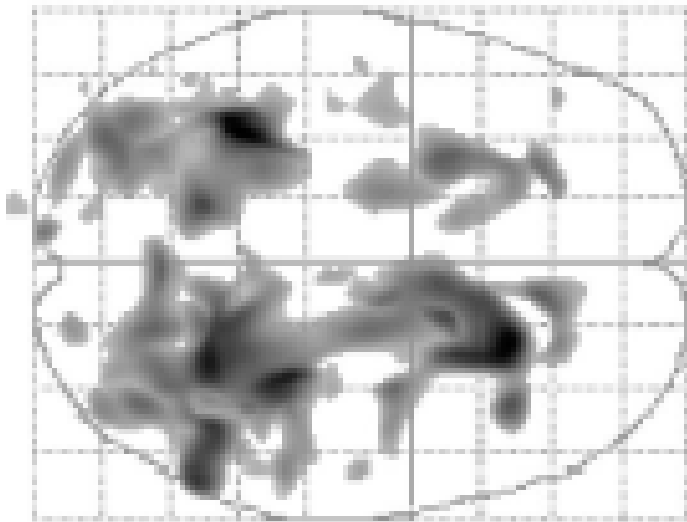
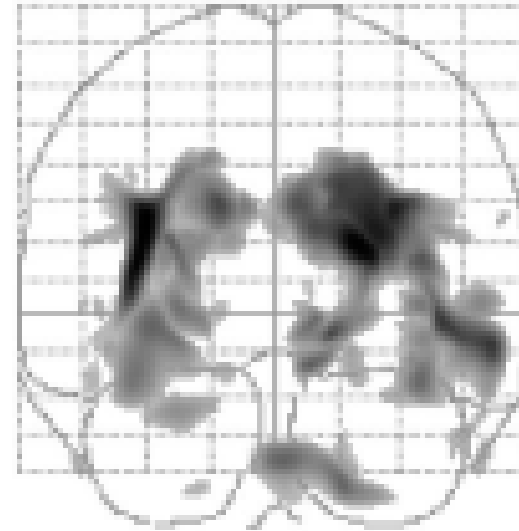
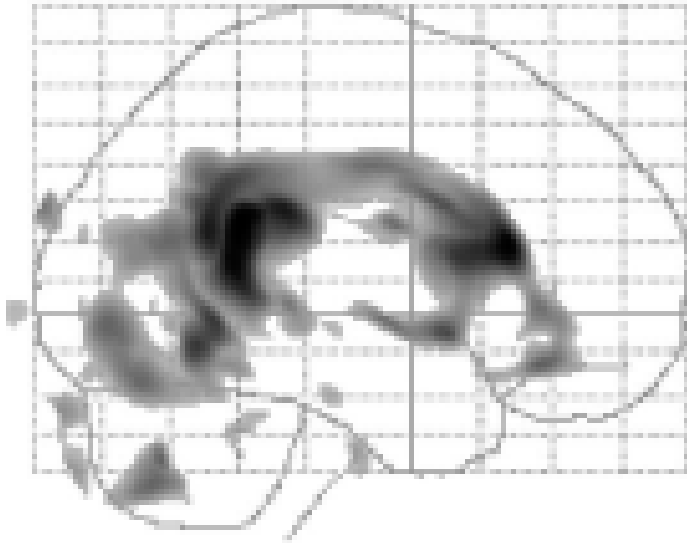
Macey, P., et al. *Sleep*, 31: 967-977, 2008.

Kumar, R., et al. *Depression and Anxiety*, 26: 480-491, 2009.



Ronald M. Harper, Ph.D.
Brain Research Institute, UCLA.
Los Angeles, California.

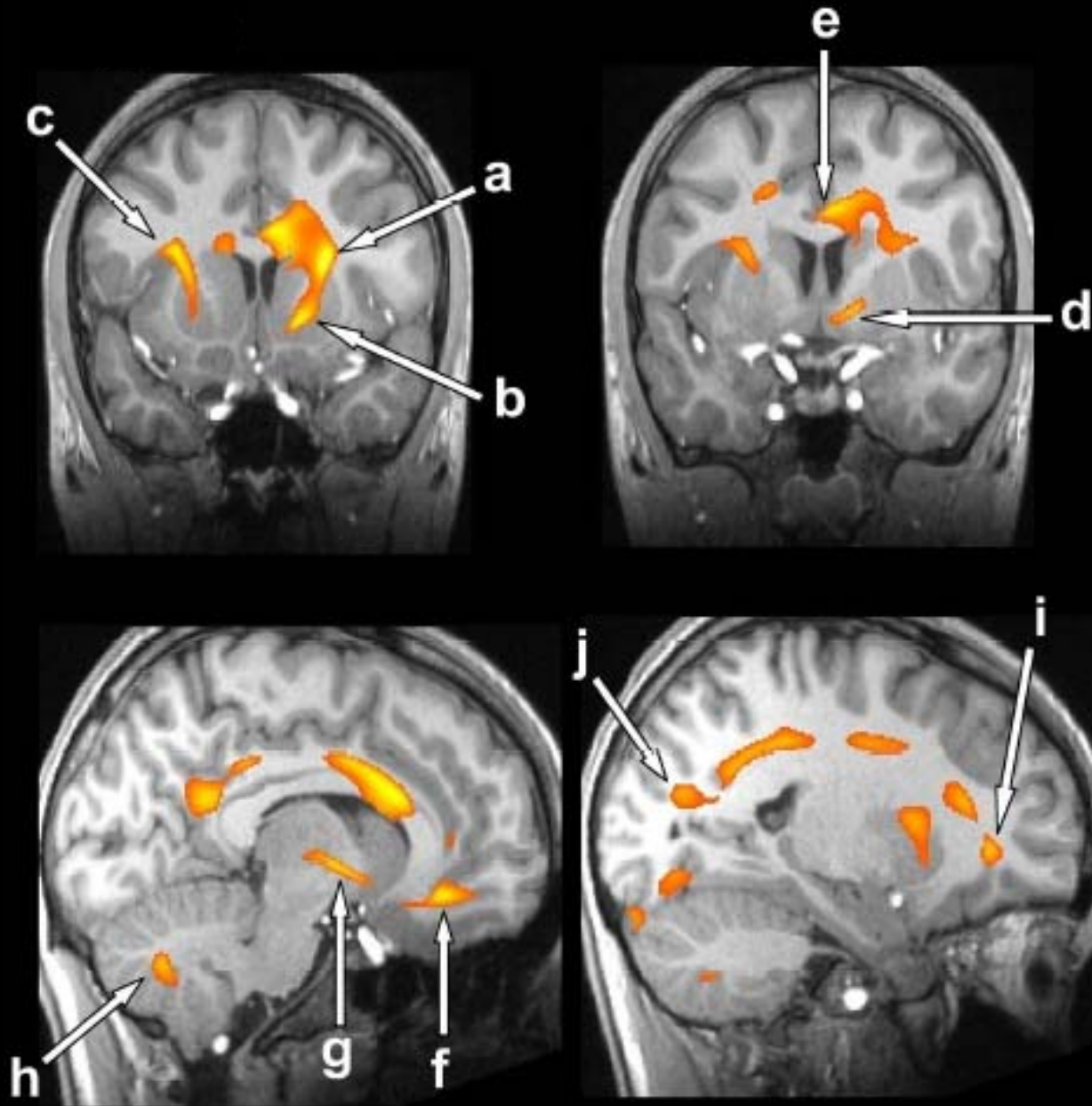
Areas of Neuronal Damage in CCHS vs Controls



T2 differences between CCHS and Controls. High T2 values indicate absence of fiber development, diminished myelination, or decreased cell density.

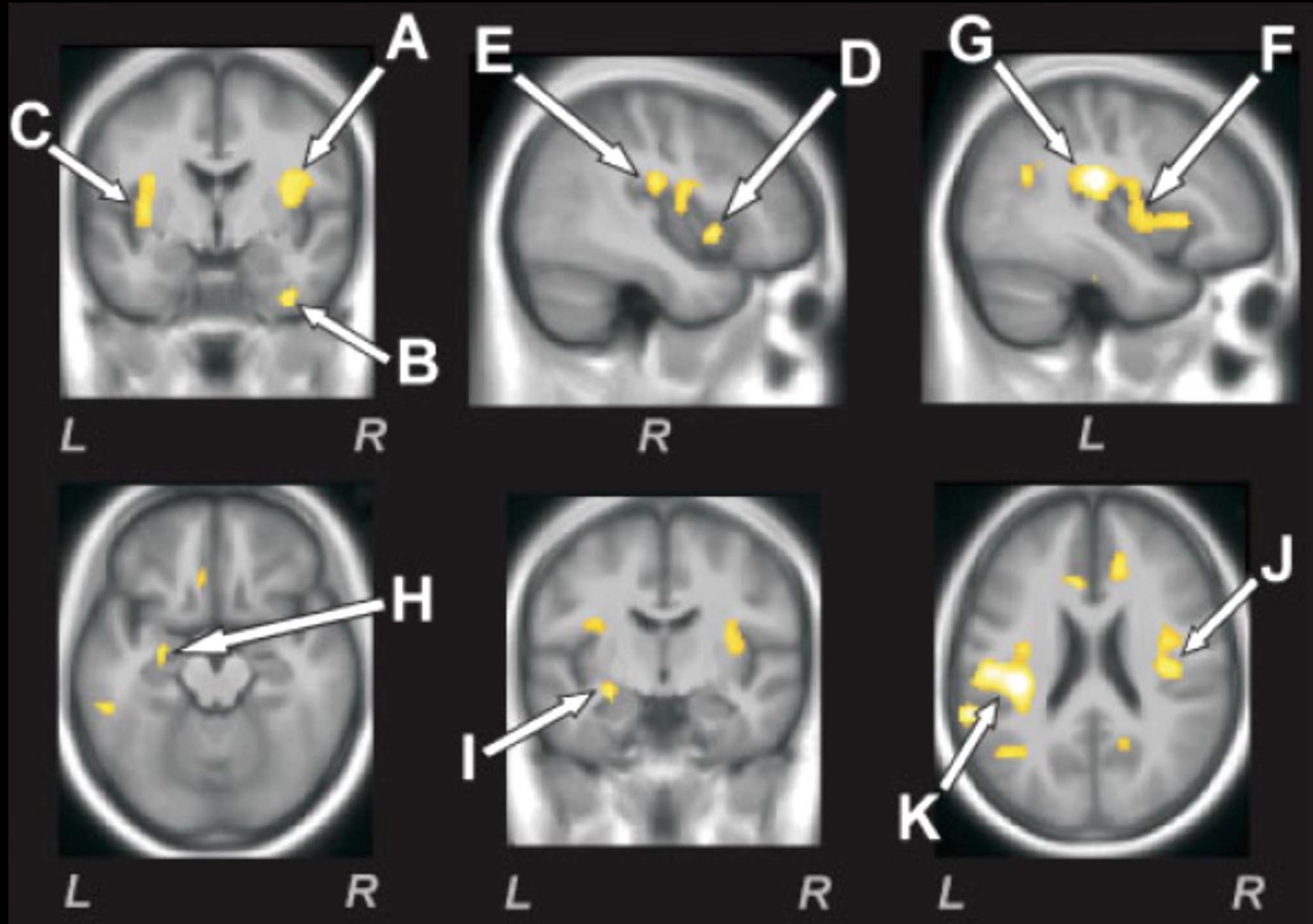
Kumar, R., et al. *J. Compar. Neurol.*, 487: 361-371, 2005.

Deficits in Basal Ganglia, Limbic and Cortical Structures in CCHS vs Controls



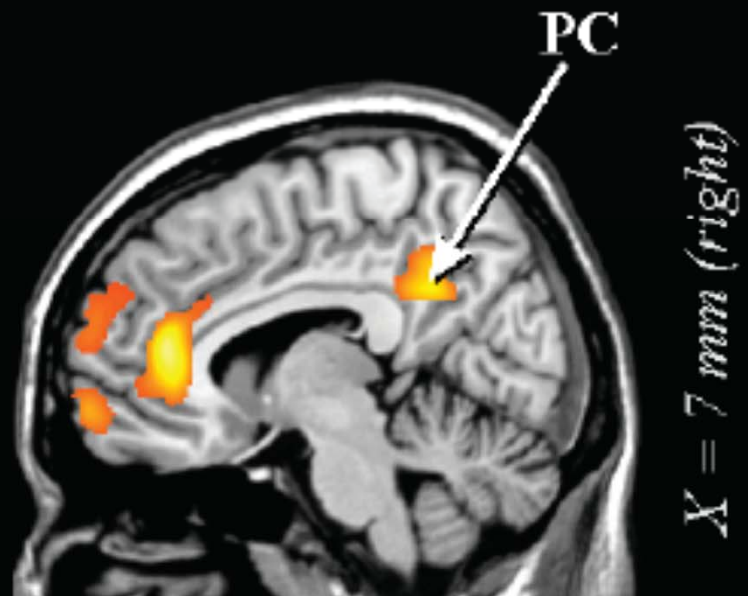
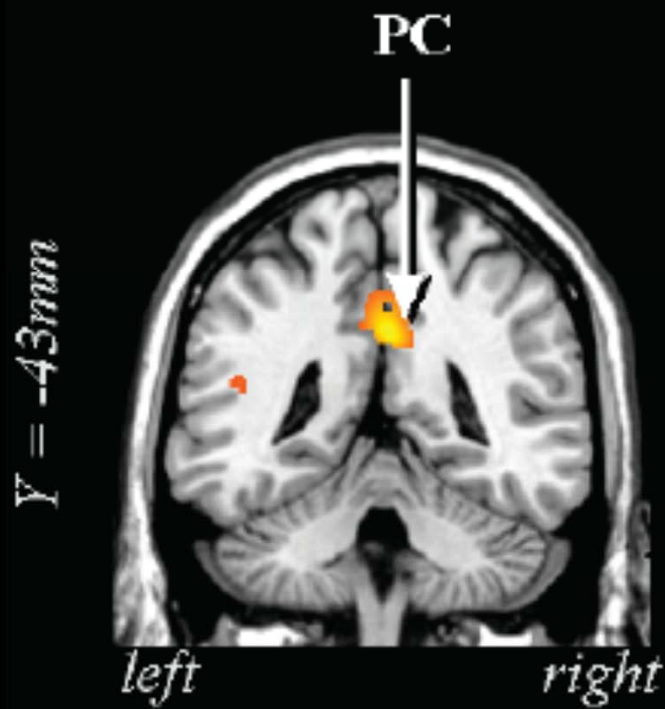
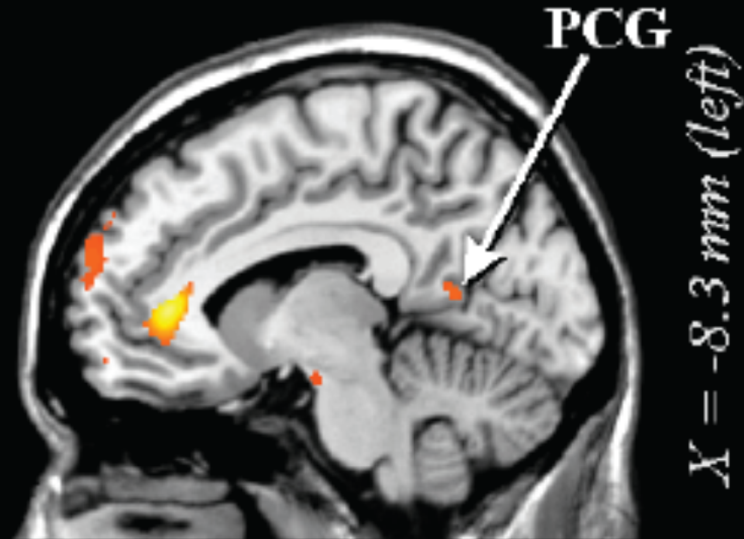
Kumar, R., et al. *J. Compar. Neurol.*, 487: 361-371, 2005.

Deficits in Hippocampus, Amygdala, and Cortical Structures in OSAS vs Controls



Kumar, R., et al. *Depression and Anxiety*, 26: 480-491, 2009.

Posterior Cingulate in OSAS vs Controls



Macey, P., et al. *Sleep*, 31: 967-977, 2008.

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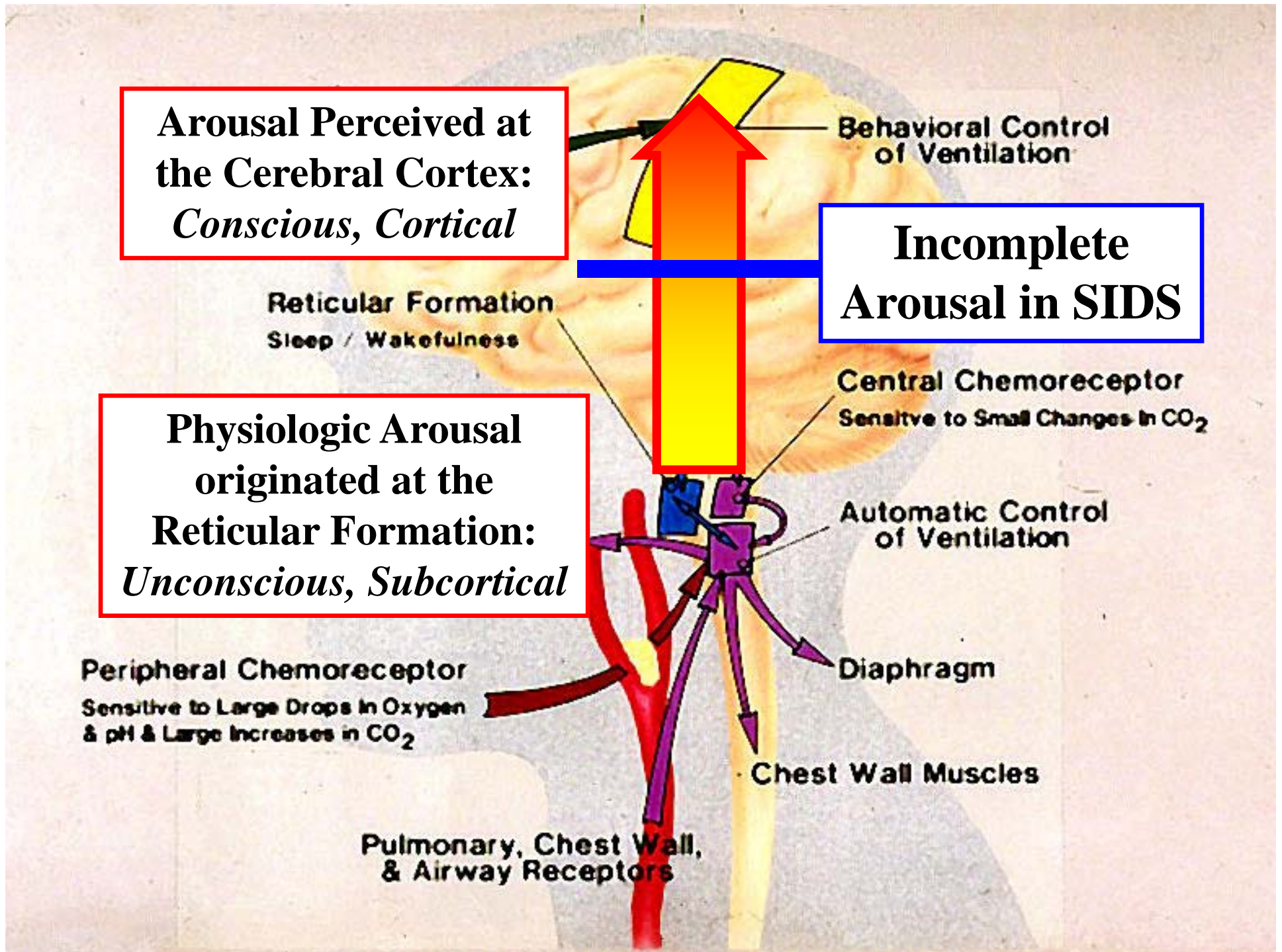
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Diaphragm

Chest Wall Muscles

Pulmonary, Chest Wall,
& Airway Receptors



Cardiorespiratory Interaction

- Hypoxia causes neuronal damage.
- Autonomic nervous system damage may exacerbate the profound effects of breathing on heart function.
- This may cause cardiovascular collapse via autonomic nervous system dysfunction.
- Such cardiovascular collapse may cause SIDS.

Harper, R.M, et al. *J. Neurophysiol.* 93: 1647-1658, 2005.

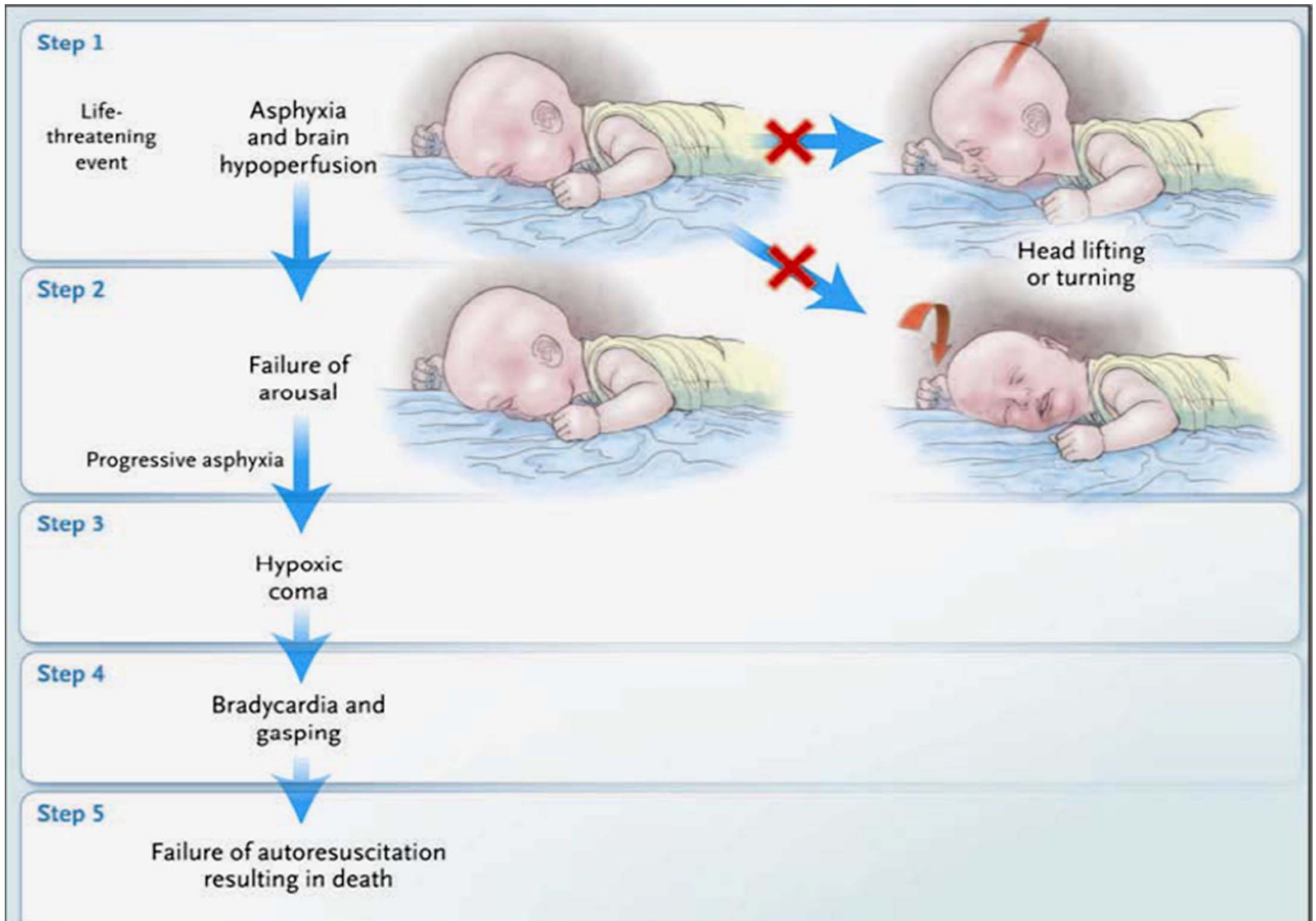
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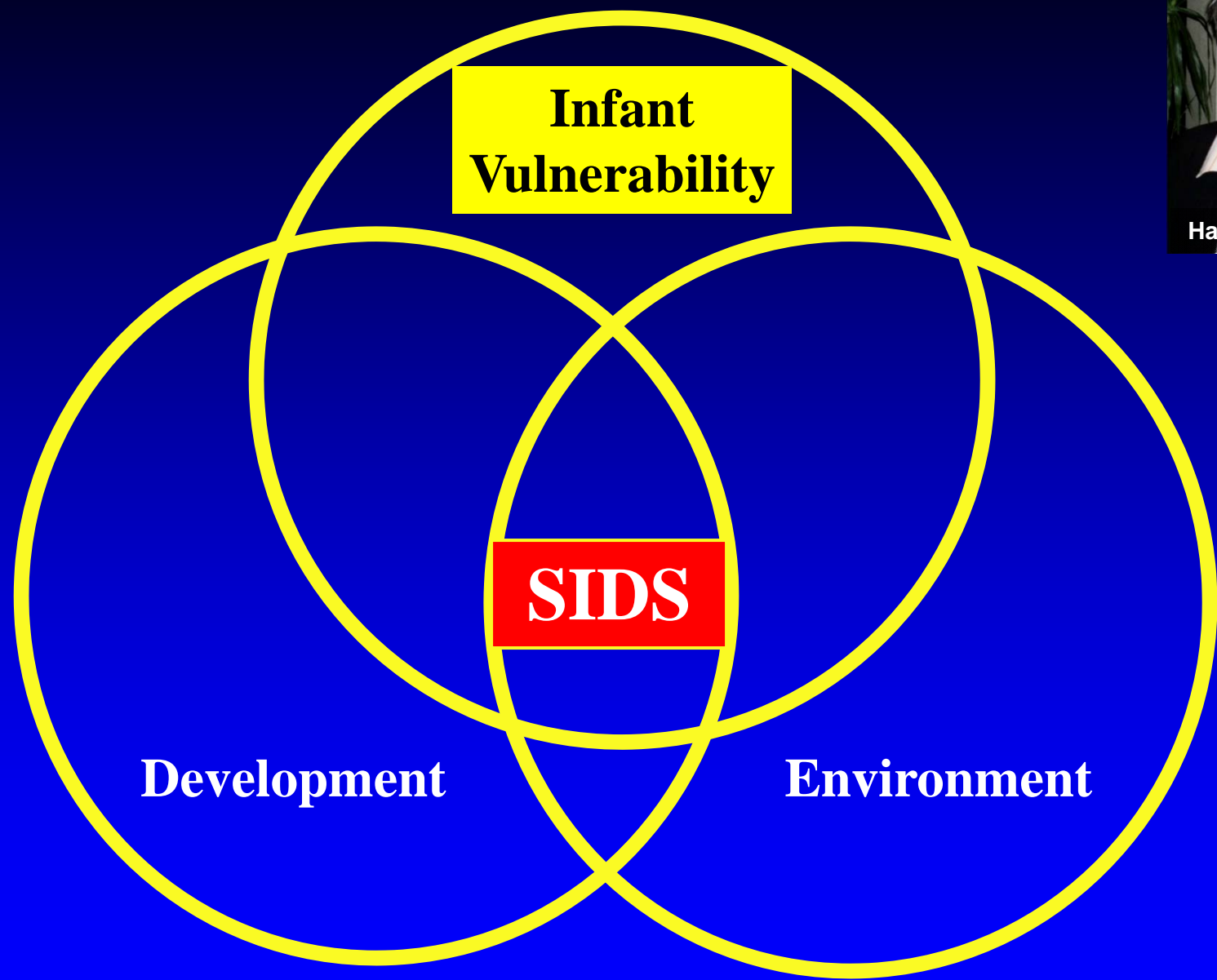
Ronald M. Harper, Ph.D.
Brain Research Institute, UCLA.
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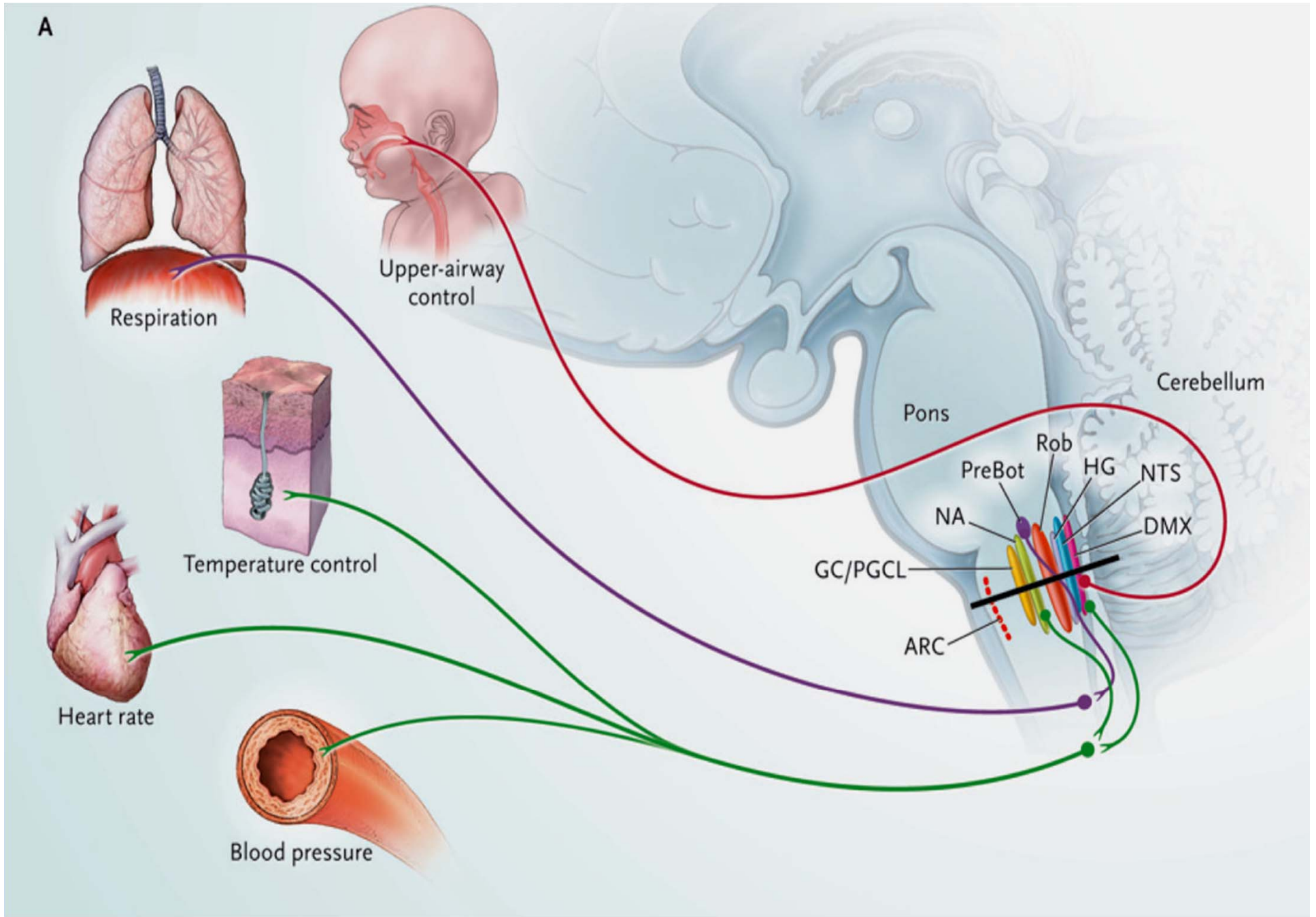
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Brainstem Neurotransmitters in SIDS



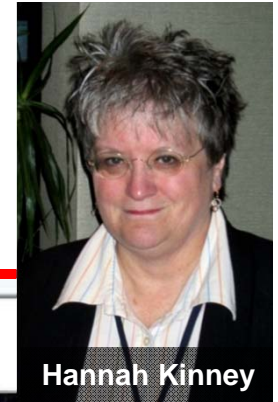
Professor Hannah Kinney.
Neuropathologist.
Harvard Medical School.

- Brainstem is the *life support* portion of the brain.
- Autopsy study found decreased serotonin (5-HT) and serotonergic neurotransmitter receptor binding activity in SIDS brainstems *vs* controls.
- Basic elements of serotonin synthesis, neurotransmission, and neuronal firing, of 5-HT are abnormal.

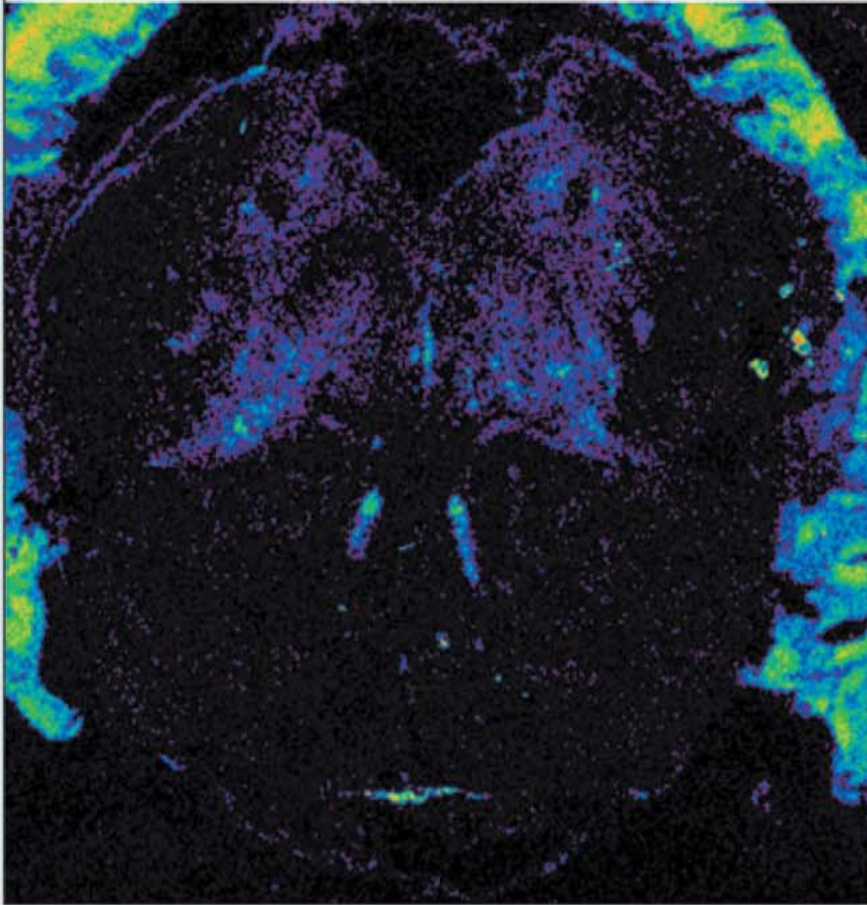


Panigrahy, A., et al. *J. Neuropath. Exp. Neurol.*, 59: 377-384, 2000.
Kinney, H.C., et al. *J. Neuropath. Exp. Neurol.*, 60: 228-247, 2001.
Kinney, H.C., et al. *J. Neuropath. Exp. Neurol.*, 62: 1178-1191, 2003.
Paterson, D.S., et al. *J. Amer. Med. Assoc.*, 296: 2124-2132, 2006.
Duncan, J.R., et al. *J. Amer. Med. Assoc.*, 303: 430-437, 2010.

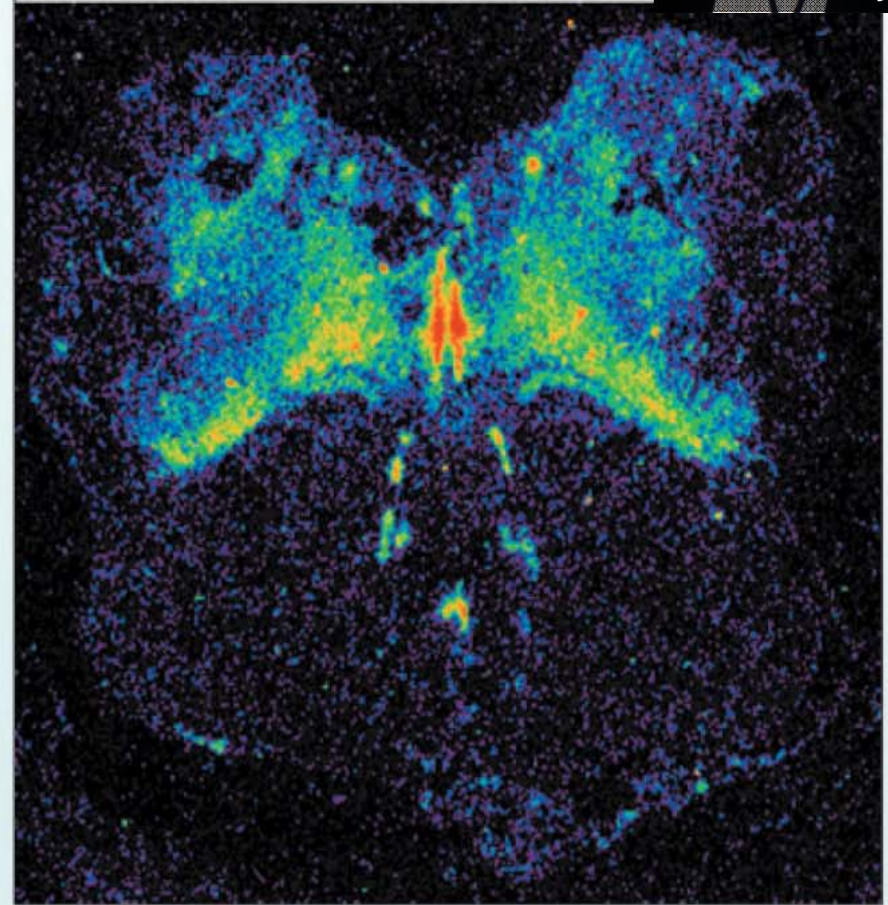
5-HT_{1A} Receptor Binding Density in the Mid-Medulla from SIDS vs Control



B Infant with Sudden Infant Death Syndrome



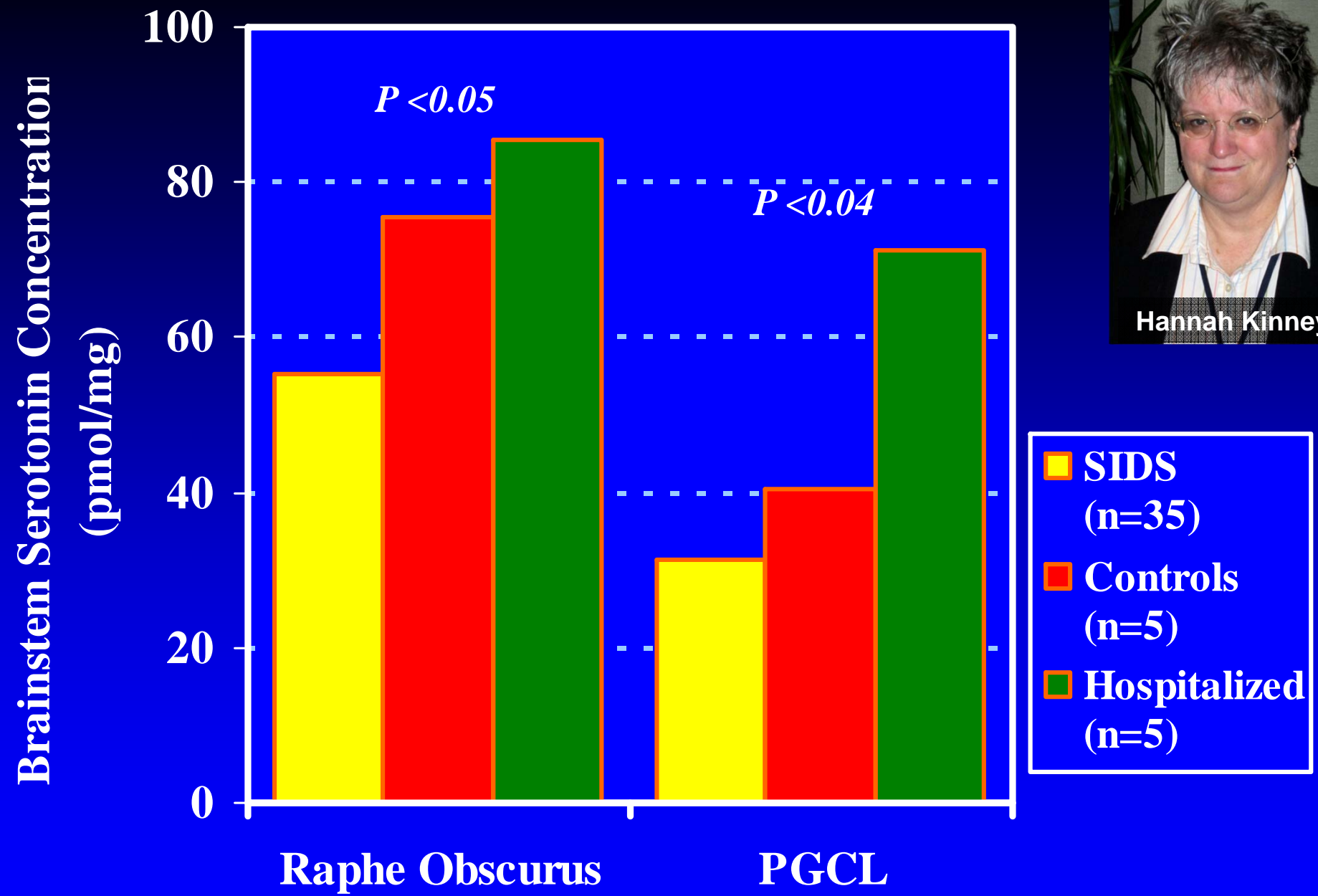
C Control Infant



Paterson, D.S., et al. *J. Amer. Med. Assoc.*, 296: 2124-2132, 2006.



Hannah Kinney



Duncan, J.R., et al. *J. Amer. Med. Assoc.*, 303: 430-437, 2010.

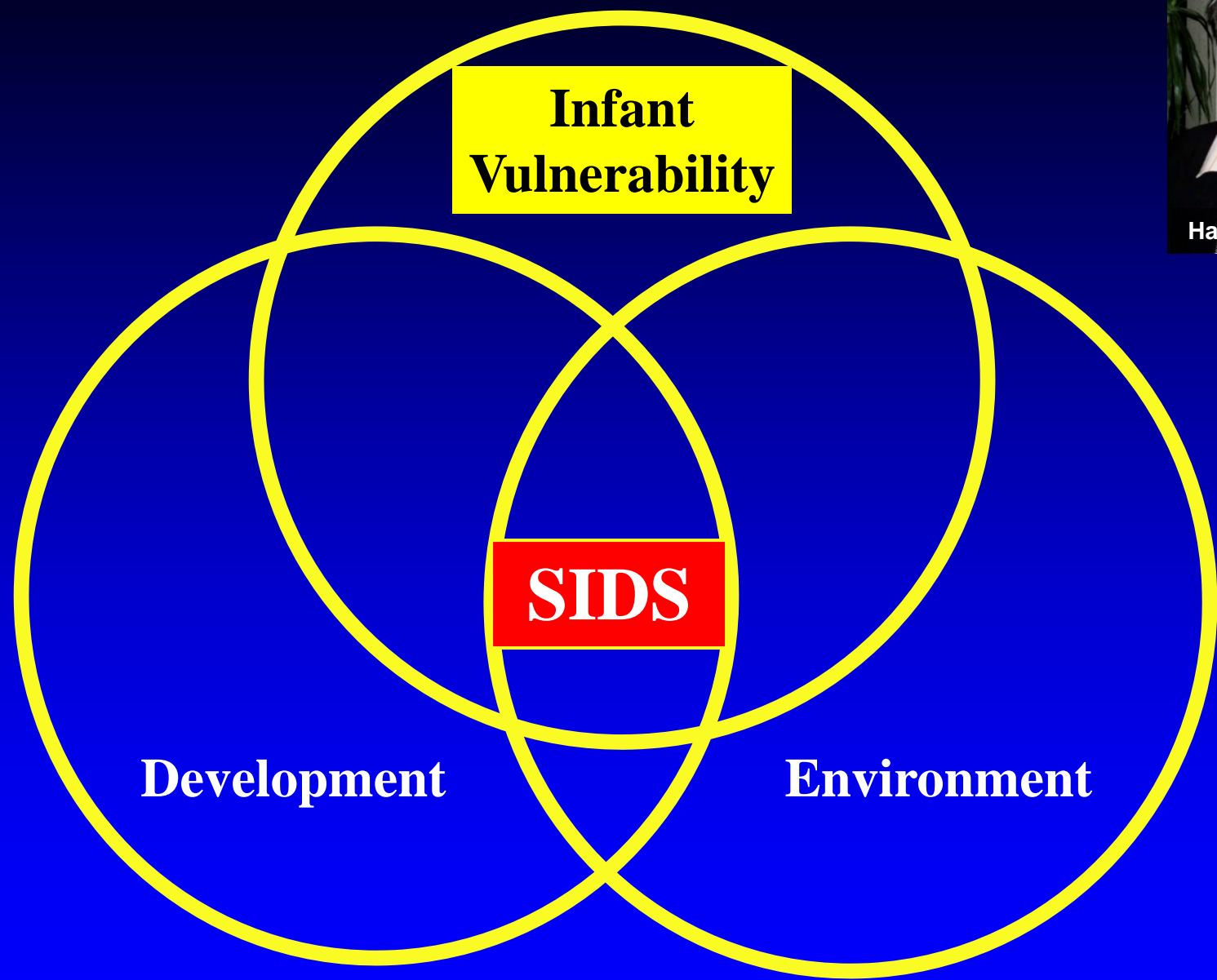
Brainstem Neurotransmitters in SIDS



- 5-HT abnormalities may be developmental in origin.
- SIDS victims may have abnormal neurologic control of cardiac, respiratory, and/or arousal function.
- Confirms a biological basis for SIDS.
- Supports risk reduction strategies.



Panigrahy, A., et al. *J. Neuropath. Exp. Neurol.*, 59: 377-384, 2000.
Kinney, H.C., et al. *J. Neuropath. Exp. Neurol.*, 60: 228-247, 2001.
Kinney, H.C., et al. *J. Neuropath. Exp. Neurol.*, 62: 1178-1191, 2003.
Paterson, D.S., et al. *J. Amer. Med. Assoc.*, 296: 2124-2132, 2006.
Duncan, J.R., et al. *J. Amer. Med. Assoc.*, 303: 430-437, 2010.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

↓ brainstem serotonin:
Autonomic Dysfunction
Disrupting
Cardiorespiratory Control

Infant
Vulnerability

SIDS

Development

Environment



Hannah Kinney

Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

↓ brainstem serotonin:
Autonomic Dysfunction
Disrupting
Cardiorespiratory Control

**Infant
Vulnerability**

Respiratory Dysfunction
(Hypoxia) → Cardiovascular
Collapse (Shock)

SIDS

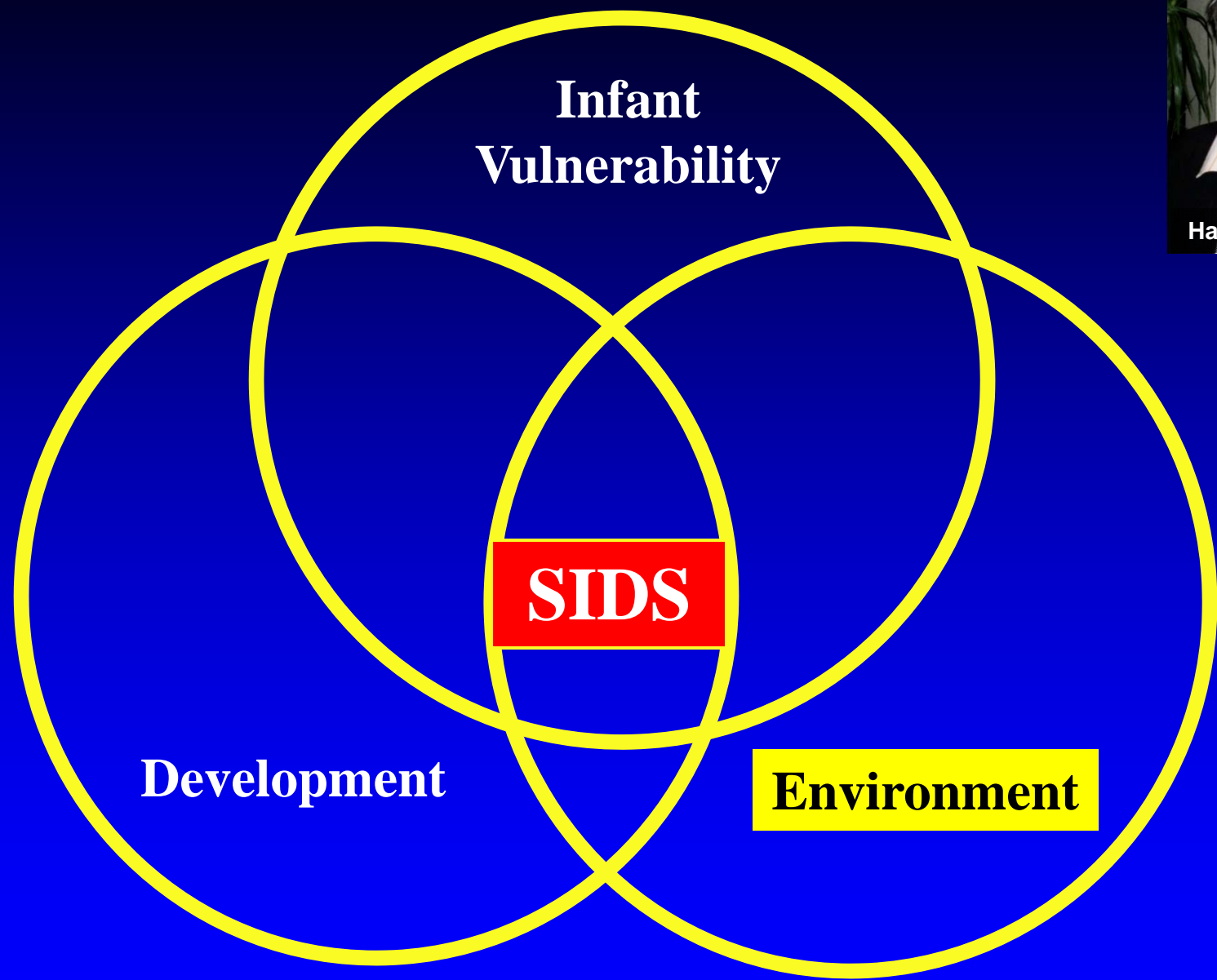
Development

Environment



Hannah Kinney

Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

Defining the cause of SIDS has been a real roller coaster ride:

- From blaming parents, *Ancient Greece and Rome and Middle Ages.*
- To natural causes, *Late 1800's and early 1900's.*
- To blaming parents again, *Early to mid 1900's.*
- To natural causes again, *Late 1900's and early 2000's.*
- Now to unsafe, accidental causes.



Russell-Jones, D.L., *Arch. Dis. Child.*, 60:
278-281, 1985.

Spectrum of Infant Deaths

**Known
Cause of
Death**

**Biology
Interacts
with
Environment**

**“True”
SIDS**

**Clear evidence of
suffocation,
entrapment, etc.**

**Some Risk Factors,
but would not cause
death in all infants.**

**No Risk
Factors.**

Dx: Accidental

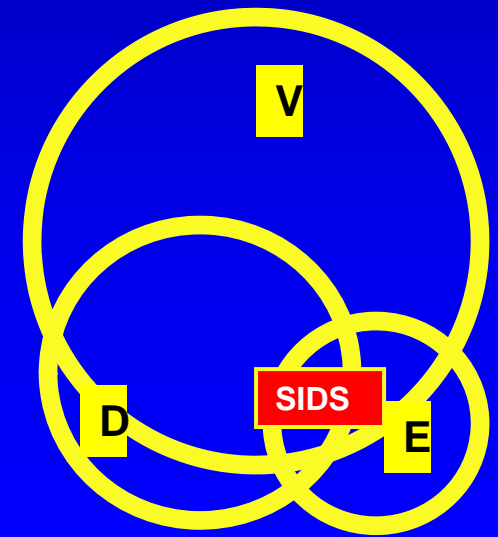
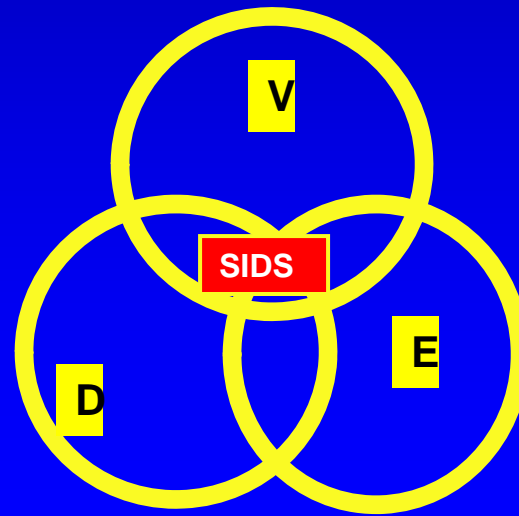
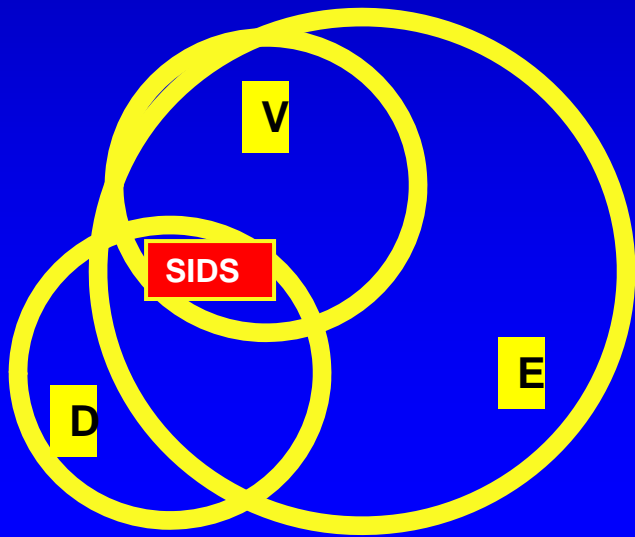
Dx: Variable

Dx: SIDS

**Known
Cause of
Death**

**Biology
Interacts
with
Environment**

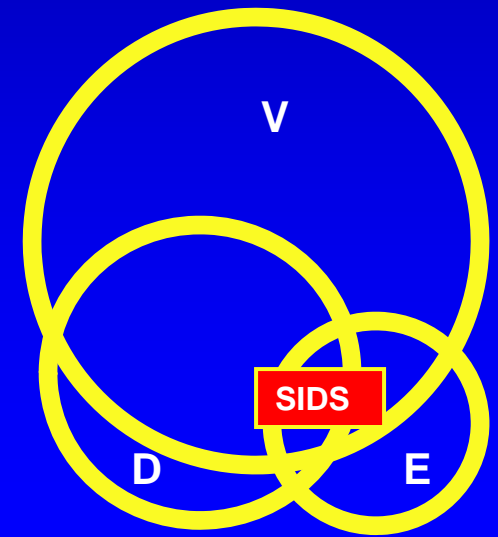
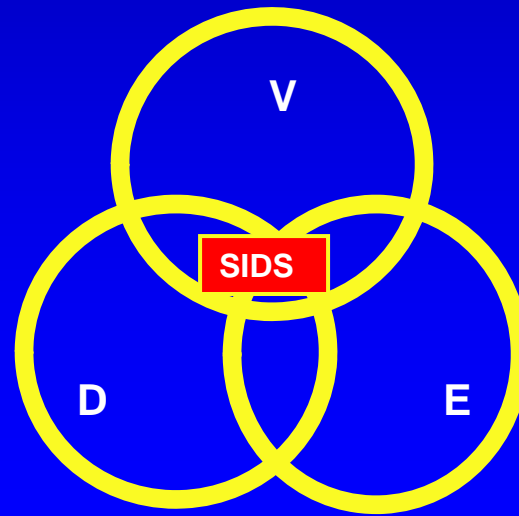
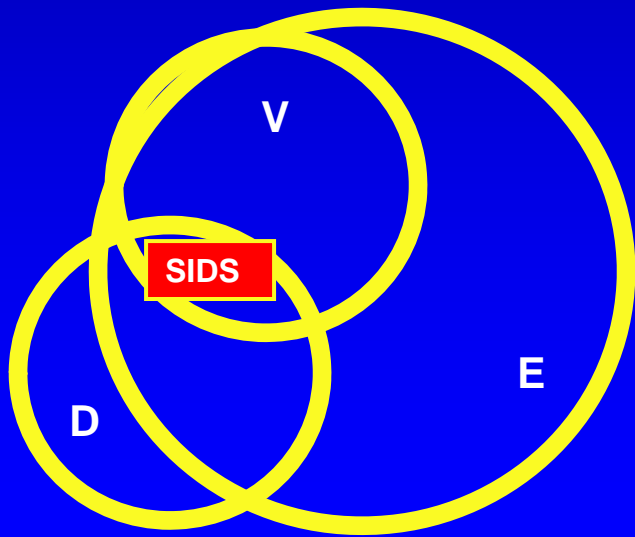
**“True”
SIDS**



**Known
Cause of
Death**

**Biology
Interacts
with
Environment**

**“True”
SIDS**



**Known
Cause of
Death**

**Biology
Interacts
with
Environment**

**“True”
SIDS**

**Clear evidence of
suffocation,
entrapment, etc.**

D

E

Dx: Accidental

**Some Risk Factors,
but would not cause
death in all infants.**

D

E

Dx: Variable

**No Risk
Factors.**

D

E

Dx: SIDS



**Coroners' Curriculum Development Committee
California State Coroners' Association**





SIDS Summit 2011



- **32 Coroners and Pathologists from around California attended.**
- **Working conference to explore whether or not it is possible to achieve better consistency between counties on diagnosing the cause and manner of death in babies dying suddenly and unexpectedly.**
- **Attendees voted on cause of death and manner of death on a number of cases, to bring out areas of common ground and of difference.**

**SIDS Summit 2011. California State Coroners' Association.
Studio City, California. October 19, 2011.**



SIDS Summit 2011



“Pristine SIDS” Case.

| Cause of Death | % |
|----------------|----|
| SIDS | 56 |
| Undetermined | 22 |
| SUID | 16 |
| Asphyxia | 6 |

| Manner of Death | % |
|-----------------|----|
| Accidental | 0 |
| Homicide | 0 |
| Natural | 63 |
| Undetermined | 38 |

Some pathologists were persuaded to use “SUID” because it is recommended by the CDCP.

**SIDS Summit 2011. California State Coroners' Association.
Studio City, California. October 19, 2011.**



SIDS Summit 2011



- Other cases were reviewed which had a variety of findings.
- Complete consensus was not achieved on any case, but those with a positive finding had better agreement.
- The conference illustrated the complexity of cases Coroners currently see.
- Increased observations revealed more questions.
- Difficult to come to a definitive diagnosis.
- Achieve “probable cause” or “certainty”?

**SIDS Summit 2011. California State Coroners' Association.
Studio City, California. October 19, 2011.**

**Known
Cause of
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E

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D

E

Dx: Variable

**No Risk
Factors.**

D

E

Dx: SIDS

Diagnosis of Sudden Unexpected Death in Infancy in California

- **Coroners and Medical Examiners in different counties use different diagnoses (names) for unexplained infant deaths which are sudden and unexpected.**
- **SIDS, Undetermined, SUID, SUDI, etc.**
- **These all mean the same thing.**
- **Public health services should be provided to all.**
- **Parents should be counseled that these diagnoses all mean the same thing.**

**SIDS Summit 2011. California State Coroners' Association.
Studio City, California. October 19, 2011.**

Sudden Unexpected Death in Infancy: Challenge to California SIDS Community

- **As authorities in health care, we need to convey the message that these differing diagnoses are equivalent!**
- **Support should be provided to all families.**
- **Coroners and Medical Examiners should voluntarily refer all families to MCAH/Public Health Nurses.**
- **MCAH should provide grief and education services to families of all “presumed SIDS”.**
- **Support services help families work through the death of their infant and are critical and beneficial.**

California SIDS Advisory Council, August 14, 2012.

California Department of Public Health, December 17, 2012.



**When theories compete in
profusion
Then, the experts conclude
in confusion,
There'll be flaws in all laws
Of this unexplained cause
Till the problem is solved
by exclusion.**



*Lady Sylvia Limerick
SIDS Parent
1976*

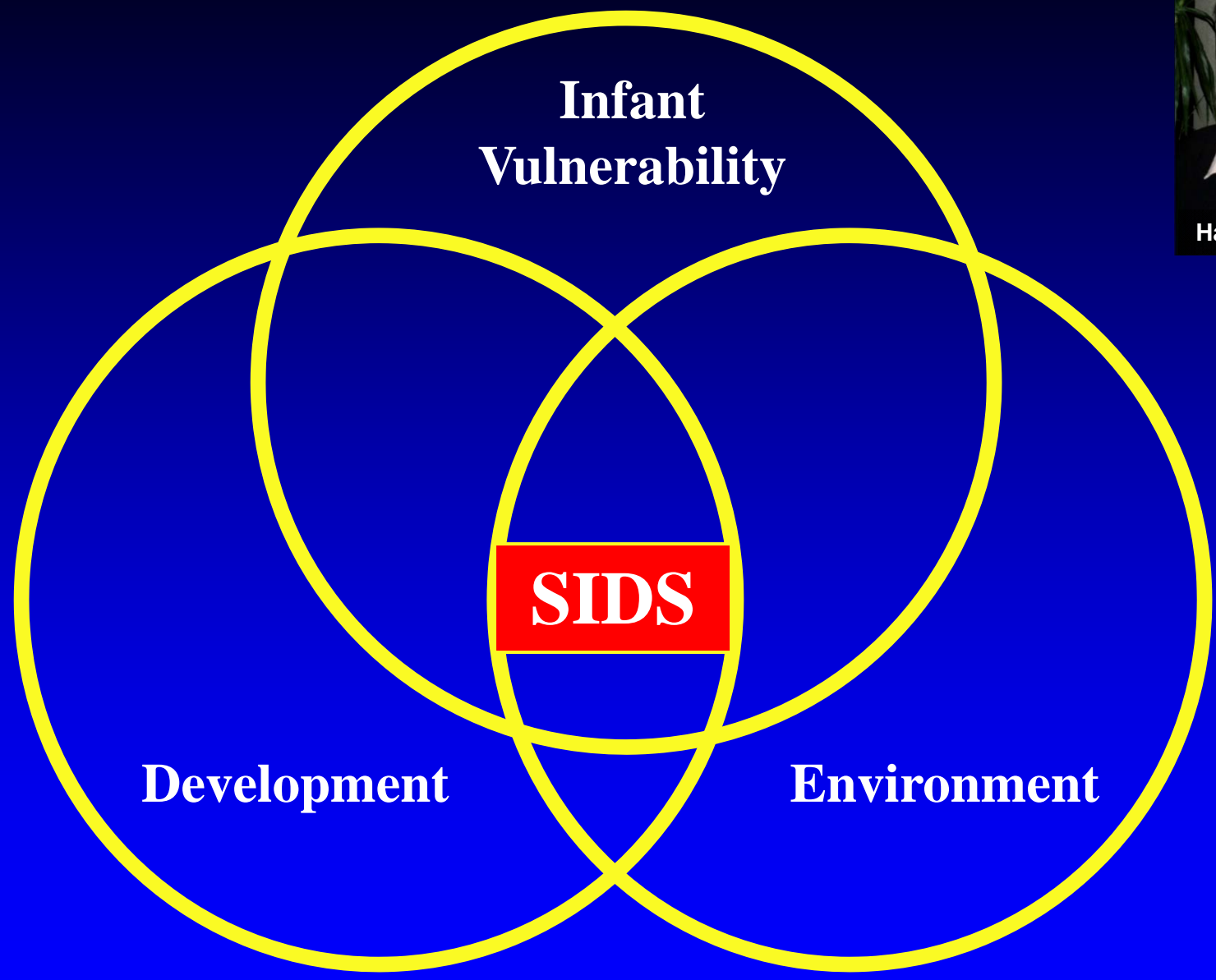
Russell-Jones, D.L. *Arch. Dis. Child.*, 60: 278-281, 1985.

WARNING

The cause of SIDS is not yet known.

**This information has not been proved
to be the cause of SIDS.**

**However, I have attempted to give
you some idea about some current
directions of SIDS research.**



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

Sudden Infant Death Syndrome

- **Most common cause of sudden infant death between the ages of 1-month and 1-year.**
- **Cause remains unknown.**
- **Can not be predicted in infants prior to death.**
- **Reduction in SIDS in populations through public health intervention.**

A black and white graphic with a red prohibition sign over the text 'SIDS'. The text 'SIDS' is written in a bold, black, sans-serif font. A thick red diagonal line crosses through the text from the top-left to the bottom-right. The entire graphic is set against a white circular background, which is itself centered on a black square background.

SIDS